BACKLOG OF PATENT APPLICATIONS AT THE U.S. PATENT AND TRADEMARK OFFICE AND ITS EFFECT ON SMALL HIGH-TECHNOLOGY FIRMS

HEARING

BEFORE THE

SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

OF THE

COMMITTEE ON SMALL BUSINESS HOUSE OF REPRESENTATIVES

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BACKLOG OF PATENT APPLICATIONS AT THE U.S. PATENT AND TRADEMARK OFFICE AND ITS EFFECT ON SMALL HIGH-TECHNOLOGY FIRMS

TUESDAY, MARCH 29, 1988

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON REGULATION AND
BUSINESS OPPORTUNITIES,
COMMITTEE ON SMALL BUSINESS,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:00 a.m., in room 2359-A, Rayburn House Office Building, Hon. Ron Wyden (chairman of the subcommittee) presiding.

Present: Chairman Wyden; Representatives Price and Gallegly.

Chairman WYDEN. The subcommittee will come to order.

Today, we are going to examine the problems the U.S. Patent and Trademark Office faces in processing biotechnology patent applications in our country.

To the uninitiated, this might sound like the harmless disorganization of the bureaucratic backwater, but as today's hearing will show, nothing could be further from the truth.

Patents are always serious business. When it comes to cutting-edge technology, the patent approval process can shape or warp the future of an entire fledgling industry. Simply put, approved patents are the financial and legal backbone of any biotechnology firm and the Patent Office's current troubles with applications processing have clouded the future of this highly promising domestic industry.

Current projections point to an amazing financial future for biotechnology. Domestic sales in fields ranging from medicine to agriculture are supposed to increase 1,800 percent in the coming decade, to around $13 billion annually. The international market is projected at more than three times that.

But the ground work for the future is being laid right now. The burgeoning biotechnology industry is currently in a crucial phase of its young life. Witness, for example, the recent explosive growth in patent applications. In January 1985, a little more than 3,900 patent applications were pending, a mere 2½ years ago. By August 1987, over 7,800 were awaiting action.

Unfortunately, the Patent Office, one of the most important gatekeepers in the biotechnology field, has not proven equal to the challenges posed by the industry's rapid expansion. During the January 1985 to August 1987 period, the gap between total pending

applications and final decisions continued to widen, despite a 100-percent increase in applications disposed of during that period.

By its own admission, the Patent Office biotechnology section is in trouble, and the situation is getting worse. The backlog is lengthening, and examiner recruitment and retention problems persist. Biotechnology patent applicants cope with the 4- to 5-year approval process as best they can.

The big well-capitalized firms are in a better position to play the waiting game. They may possibly have the cash to hold out. But, particularly for the small firms in our country, the delays can be crippling and options are few.

Some concerns, like Genentech, take the risk of marketing their inventions without the protection of a patent. Let us make no mistake about it, that strategy is risky. We will explore its costs with one of today's witnesses, the chief executive officer of AMGEN, a company whose product may have been stolen by a foreign competitor while part of its patent application languished.

Others hold off making their inventions public, pending patent approval, but those companies suffer the risk of lost financing and forsaken opportunity. Particularly for the small U.S. biotechnology company, those that are staking their future on just one breakthrough, the current state of affairs at the Patent Office is a crippling hurdle, and, as the subcommittee is going to hear this morning, the state of the Patent Office biotechnology section not only hurts the industry, but it retards scientific research in biotechnology fields as well.

In today's hearing, the subcommittee is going to be attempting to identify and understand the root causes of the Patent Office's difficulties. Subcommittee staff has obtained documents that indicate Patent Office management requested additional funds for its biotechnology department for the current fiscal year, but in one of the more penny-wise and pound-foolish decisions I have seen in the time I have been in Congress, the request was turned down flat by the Office of Management and Budget and Personnel Management.

Now, it ought to be noted that the Patent and Trademark Office is not one of Government's more lavish outposts. In fact, its biotechnology section is kind of like the 19th Century meeting the 21st. Like the rest of the Patent Office, it barely is computerized.

In a recent visit, subcommittee staff found nearly 50 supermarket-style shopping carts overflowing with patent applications in the agency's mailroom. The checks for the filing fees were still attached. Some were weeks old. Overworked biotechnology examiners are woefully underpaid by the standards of the industry, which is only too eager to hire away people with such valuable skills.

Over the past 2 years, 21 employees have left the office's three major biotechnology examining units, amounting to staff turnover of about 50 percent, a most disturbing figure.

In the most severely affected biotechnology examining units, it now takes an average of 27 months just to open an application file and then another 25 months to award or deny a patent. Subcommittee staff reviewed one examiner's workload, and he told them in his own words that he had finally made the turn. This meant that, in effect, he had opened all his mail from 1985. This is considered something of an accomplishment in the biotechnology unit, which

is far behind the Patent Office's overall 19.4-month average processing time.

These serious deficiencies are weighing heavily on the still-fragile field of biotechnology. This subcommittee wants to see the U.S. Patent Office achieve its twin goals of efficiency and quality because a decline in quality, in particular, would have a disastrous impact on the smaller competitors in this field.

With so much at stake scientifically, ethically, and economically, these goals must go hand-in-hand. Quality and efficiency must be an effective team. Biotechnology is at the very frontier of economic growth in our country. This Congress must not sit by and allow this exciting field to drift into a regulatory never-never land.

A distinguished group of witnesses joins us today. Some of them have traveled great distances, and I am particularly pleased that an expert from my own home State of Oregon, Oregon State University, will be here to discuss the impact of this field on the university community, in particular.

Before we go to our witnesses, I want to recognize my colleagues.

Let me start with the gentleman from California, Mr. Gallegly. We welcome you to the subcommittee and appreciate your interest.

Mr. GALLEGLY. Thank you very much, Mr. Chairman, and members of the subcommittee.

I appreciate the opportunity to make a statement regarding the backlog of patent applications at the U.S. Patent and Trademark Office.

Mr. Chairman, the backlogging of patent applications is of catastrophic proportions for small high-technology firms as well as university research. This unfortunate delay is of an increasing concern to small firms, such as AMGEN, which is in my district. In addition, many other small firms, whose business foundation rests on the idea of patentable ideas, are affected by this delay in the application process.

Not only are these enterprises at risk, but the entire biotechnological field suffers while struggling to expeditiously research and develop methods and technology which can benefit our society as a whole.

Mr. Chairman, recognition of any problem is the first step toward finding an effective solution. It is my understanding that the Office of Patent and Trademark has made an effort toward improving the quality of its patent examinations as well as attracting and retaining the personnel necessary to reduce the pendency time of patent applications.

However, it appears that further steps need to be taken to redress the patent backlog problem. This need may magnify based on the recent growth of the biotechnology field in the next several years.

Current projections indicate that biotechnology sales in the U.S. market will total $650 million alone this year. That figure is expected to double in the next 10 years.

Mr. Chairman, it is evident that the biotechnology industry is an essential component of the U.S. market, providing investment opportunities, a significant number of jobs, and essential technology to urgent problems facing our society.

Because of this growing role in our society, I believe we must make a concerted and expeditious effort to meet the needs of the industry with regard to patent applications. I come here today, not with a solution, but with a conviction that we must work—Congress the U.S. Patent Office, and industry—to find solutions which serve to eradicate this backlog problem.

I look forward to your suggestions as to what that solution might be, and I am confident that an alternative exists which can accommodate all of you present here today.

Thank you very much, Mr. Chairman.

Chairman WYDEN. I appreciate the gentleman's statement, and look forward to working with him.

Let me recognize the gentleman from North Carolina, who has a long-standing interest in this subject and has been most helpful in the development of our inquiry today, Mr. Price.

Mr. PRICE. Thank you very much, Mr. Chairman.

I want to commend you for convening this hearing on this critical problem facing our Nation's biotechnology industry—the U.S. Patent Office's inefficiency and delay in the processing of patent applications.

I am especially pleased that we will be hearing today from Dr. Phillip Carter, who resides in the district I represent, the 4th District of North Carolina, and who will be testifying on our second panel.

Dr. Carter is currently associate vice chancellor for research at North Carolina State University. Furthermore, and, crucial for today's hearing, he is the director of the university's biotechnology program.

In that capacity, he has been able to experience firsthand how the backlog in the processing of biotechnology patents affects the academic community and small businesses involved in biotechnology research and development.

I am very pleased that our subcommittee has the opportunity today to hear from this fine scholar and administrator from one of our distinguished universities.

I know we will benefit from hearing his views as well as the views of the other witnesses who will be on the two panels.

Thank you, Mr. Chairman.

Chairman WYDEN. I Thank the gentleman.

Let us bring forward our first panel. Mr. Donald J. Quigg, Commissioner, U.S. Patent and Trademark Office, the Department of Commerce, and I gather you will be accompanied by Mr. Tegtmeyer. Please come forward, and we welcome both of you at this time.

Gentlemen, we will make a copy of your prepared remarks a part of the record in their entirety, and in the interest of time, if you could summarize your principal concerns today, that would be very helpful to the subcommittee.

TESTIMONY OF DONALD J. QUIGG, ASSISTANT SECRETARY AND COMMISSIONER OF PATENTS AND TRADEMARKS, ACCOMPANIED BY RENE D. TEGTMEYER, ASSISTANT COMMISSIONER

Mr. QUIGG. Thank you, Mr. Chairman and members of the subcommittee.

I welcome this opportunity to testify before your subcommittee on the operation of the Patent and Trademark Office, and specifically on our plans for handling the ever-increasing number of patent applications relating to biotechnology.

Before, however, addressing these specific concerns expressed by you, Mr. Chairman, I would like to present a brief overview of the Patent and Trademark Office, its mission, and its functions.

The main functions of the Patent and Trademark Office are to administer the Patent and Trademark laws as they pertain to the granting of patents and registration of trademarks. The examination of patent applications is the largest function of the office. This work is divided among examining groups, each of which has jurisdiction over certain assigned chemical, mechanical, or electrical technologies.

At present, there are 16 examining groups, including one for exclusively handling patent applications relating to biotechnology that became operational just yesterday.

Our staff of 3,396 employees at the end of last fiscal year included over 1,400 patent examiners. The volume of applications filed has been steadily increasing over the years, and during fiscal year 1987, a record 126,597 patent applications, excluding designs, were filed, up almost 5,000 from the previous year's all-time high of 121,611.

Examiners disposed of 126,189 cases. Patents issued, excluding designs, totaled a record 82,635, up substantially from the 71,791 in fiscal year 1986.

Aware of the need to issue patents as promptly as possible, the office began a drive in 1982 to reduce to 18 months the average time for final action on a patent application. However, because of the increased workload, coupled with funding reductions under Gramm-Rudman-Hollings in fiscal year 1986, we were forced to extend our initial target date for achieving the 18-month goal to the end of fiscal year 1989. Still, biotechnology-examining groups have already reached, and are now maintaining, the 18-month goal.

Although our efforts have proved successful in the continued reduction of average pendency time for utility patents, applications in the field of biotechnology have not fared as well. When, about 3 years ago, we first realized that a backlog problem was developing in the biotechnology area, we attempted correction through the hiring of new examiners for this field. This did not, however, alleviate the problem.

After reassessing the situation about a year ago, we determined that a more drastic plan of action, including the creation of a new examining group, was necessary. We have been implementing this plan for the past year, and Assistant Commissioner Tegtmeyer recently discussed its specific points with staff members of the subcommittee.

Our action plan consists of steps that would not only shift and consolidate available examining resources, but also increase those resources for the biotechnology area from within the office and from outside.

To attract and retain good talent and to put biotechnology examiners on the par with examiners who are engineers, we want to obtain special pay rates for the new examiners in this area. To permit the most efficient application of our examining resources, we have accelerated, intensified, and enhanced technical and legal training for these examiners, and we are improving the research tools needed for the efficient production and quality examination.

With these and other points in our plan, we are addressing the problem in every way possible. However, while we are fighting the backlog problem, relief has been available all along for companies who need a patent quickly, particularly those that are thinly capitalized, and may depend on patent ownership to attract additional investment capital.

Although applications are generally examined in the order of their receipt, examination can be obtained out of turn in certain circumstances. In addition, every application that has not yet received an examination is eligible for an accelerated examining procedure if certain relatively uncomplicated procedural requirements are met.

Accordingly, patent applicants do not have to bide their time until we win the battle of the backlog. Given the existence of this program, which has a potential to reduce pendency for time-important applications significantly, we are, frankly, puzzled over its negligible use by applicants in the biotechnology area.

Of the over 5,000 biotechnology applications filed in 1987, applicants filed petitions for accelerated examination procedures in only 17 applications. As part of the program to reduce the overall pendency of patent applications to 18 months, we requested, and have received, funds since 1982 to hire additional examiners. All these and other efforts to attack our backlog and to reduce the pendency time of applications do not call for additional budget funds at this time.

Our specific plan to reduce pendency in the biotechnology area is relatively small in cost. We would, therefore, not recommend that fee revenues for patent applications be increased for this purpose. Because of the high rate of filing of biotechnology applications, we will not be able to reduce their pendency to the 18-month period by the time expected for the rest of the office.

However, by putting our present plan of improvement into effect, we can expect the new biotechnology group to reach an average pendency time of 18 months by fiscal year 1993 or 1994.

In this respect, we continue to try to serve the public by providing quality patent protection and a reasonable period of application pendency.

I might point out that as examiners are hired out of school, they are not at that point qualified to do an examination of any large number of cases. It requires a great deal of training and effort in order to put them in a position where they can independently examine an application.

Unfortunately, we do not have enough seasoned examiners to really train the number of new examiners that we would like to train. Now, of course, we could pass patent applications out as patents, but I believe that my function in the Patent and Trademark Office is to see that, to the best of our ability, no patent is issued that is not of high quality and has a high potential for being sustained by the courts.

I will be glad to answer any questions you might have.

[Mr. Quigg's statement, with attachment, may be found in the appendix.]

Chairman WYDEN. Mr. Quigg, thank you.

Mr. Tegtmeyer, did you have testimony that you wanted to offer the subcommittee?

Mr. TEGTMEYER. No, Mr. Chairman; I have nothing to add at this point to what Mr. Quigg has said.

Chairman WYDEN. Well, gentlemen, thank you very much, and let me begin with just a few questions before I recognize my colleagues.

Mr. Quigg, in a recent speech before the Industrial Biotechnology Association, you said, and I quote here, "Along the pathway between inventive conception and commercialization, the patent system has the potential for being either a bridge or a roadblock."

My question is, which is it today? Is it a bridge or a roadblock?

Mr. QUIGG. Well, I believe it may be a little bit of both. As I pointed out in my original comments here, the potential is there for an inventor or a small company to get a fast examination of his applications. So, I think, to the extent that we have small inventors, they can go in, they can file a petition for making that application special, and it will be on a fast track.

So, to this extent, I think we are a bridge. Now, obviously, to the extent that we cannot bring the backlog down as rapidly as we would like, it does pose somewhat of a roadblock.

Chairman WYDEN. Why do you think so few companies are using these special fast track procedures? It is our understanding that there are additional hoops and requirements that they have to go through, that there are problems associated with it.

It would seem to me that if it was an easy, readily available sort of tool, more would be using it. What are your thoughts on why so few small companies use it?

Mr. QUIGG. Well, my guess is that not enough attorneys are paying attention to the rules that they can operate under.

Chairman WYDEN. Well, we will ask about that as we proceed in the course of our inquiry, but it would seem to me that if it is in the small companies' financial interests, and they have told us that they want the judgments as fast as they can get them, if there is a readily available tool that is something that is a workable process for them, they are going to use it.

Now, if you think the attorneys are just not letting those companies know, we will certainly follow that up, but I am not at all convinced that is all there is.

Mr. QUIGG. I think Mr. Tegtmeyer might have some comments in this area.

Mr. TEGTMEYER. Mr. Wyden, I just might add that this is a newly emerging field of technology. A lot of the invention going on in this

field is still basic. As it matures, of course, it will evolve into more application than basic technology.

This means that in many of the cases where they are filing patent applications, they may not be ready, in many of those cases, to go on the market now, or they may not have infringers out there that they are interested in pursuing.

So, in general, we would expect there to be less interest in this area in getting patents quickly than in many other fields. It is not to say there are not instances where small companies, especially, may be interested in getting patents quickly to support their investment in the technology, and they may really need it, and in those cases, the procedure we have is there for their use.

Chairman WYDEN. Mr. Quigg, when we hear that the Patent Office has a backlog of over 7,000 biotechnology patent applications, what exactly are we referring to here?

Mr. QUIGG. We are referring to the number of applications that are actually pending from the filing date of the application until the disposal of that application, which can be one of three things. It can issue as a patent. It can be abandoned, or an appeal can be taken on it.

Chairman WYDEN. Is it correct that of the 7,000 patent applications assigned to examiners within the three principal subgroups for biotechnology, 124, 127, and 128, is it correct that within those three subgroups, that about 4,000 or about 60 percent have not received the examiner's first action?

Mr. QUIGG. I am going to ask Mr. Tegtmeyer to take that.

Mr. TEGTMEYER. For the numbers you have given, Mr. Wyden, that is essentially correct. I might point out that the 7,000 number you referred to refers to the number of patent applications pending, that were pending in those three areas in group 120. Previously, it does not count some patent applications that are in the printing process and that have not issued as patents yet, and it does not count some that are in preexamination processing prior to going to the group which we cannot count because we have not identified them at that point as belonging to the biotechnology area.

Chairman WYDEN. So, that is how you really get up to the 11,000 number, by incorporating those other applications, is that correct?

Mr. TEGTMEYER. That is correct. That would raise the number to something in that neighborhood. In addition, if you took all of the cases from the other groups that are in biotechnology-related areas and added them in, it would total to something more than the 11,000 you referred to.

Chairman WYDEN. Mr. Quigg, during the informal and formal tours that my staff made of the Patent Office, several examiners told them that the case load for biotechnology patent applications is so far backed up that several examiners are just now starting to take their first action on applications filed in early 1986.

Do you agree with your staff's assessment of how serious this backlog problem is?

Mr. QUIGG. Once again, for that detail, I will have to refer to Mr. Tegtmeyer.

Mr. TEGTMEYER. Mr. Wyden, it is correct that there are applications pending before many of the examiners, especially in the three

units in group 120, that are dated back even until late 1985 and into 1986, and those cases are quite old.

Notwithstanding that fact, the average case being acted upon, and frequently the examiners will take more recent cases out of turn because they are similar to and can be handled or searched in parallel with some of the older cases or have related issues in them is much younger than the 1985 date. The best way we can gauge that average is by taking the total backlog and dividing it by the number of cases that examiners are disposing of currently and multiplying that times 12 to get a month's pendency level to first action by the examiner. That is approximately the pendency level that you would end up with if the cases were handled strictly in turn and on a steady-state basis, and we would end up with probably something around 14 or 15 months pendency in the biotechnology area on that basis.

Chairman WYDEN. Well, we have established now that there is really a staggering backlog, and what I guess I would like to ask next is what, Mr. Quigg, do you see as the principal factors that are contributing to this backlog?

Mr. QUIGG. Well, I think the principal factor contributing to it is the inability to have enough examiners to overpower that backlog. We are——

Chairman WYDEN. Let me stop you there. Are not your examiners leaving as fast as you get new ones on?

Mr. TEGTMEYER. No, Mr. Chairman; we are losing in the biotechnology area over a period of time, not in a particular year, but over a period of time, about the same number we are losing in the rest of our examining operation. That is not to say that is a desirable attrition rate, but we are keeping ahead of it.

We plan to hire 20 people this year. We expect to lose somewhere in the neighborhood of 11, which gives us a net increase of the 9 between the two.

Chairman WYDEN. In the three biotechnology units, you are going to have a net increase of nine?

Mr. TEGTMEYER. No; I am talking about group 180 that incorporates all of the biotechnology areas. We are assembling those areas into a single group, effective this week.

Chairman WYDEN. But prior to this week—and we appreciate knowing about that—in the three major biotechnology art groups, 124, 127, and 128, have you been able to add more than you are losing?

Mr. TEGTMEYER. Yes; we have. We have been increasing the number in those areas slowly. We started back in January 1985, when we had 28 examiners. As of January 1988, we have 42 examiners in that area. That is the three art units in the now former group 120, that you were referring to.

Chairman WYDEN. All right. So, one problem is that you need more examiners. What are the other problems, Mr. Quigg?

Mr. QUIGG. Well, I think that is the major problem. We have found that solution has been very successful in other areas of the office, and it has been the factor that we have used in bringing five of the examining groups to an average pendency of 18 months.

Now, as I pointed out earlier, we cannot take these examiners or the new recruits directly out of school and expect them to do a full

caseload of work. Even with 5 years experience, we find that they are doing about 66 percent of the work which the 10-year examiner will do.

These are just managerial problems that we have to face, but I think we also have to recognize that we are in strong competition with industry for all of these people in this field.

Chairman WYDEN. I think that is a valid point, and we appreciate knowing both the examiner problem and the problem of junior people not having the expertise of more senior ones.

Mr. QUIGG. If I might add one more point. One of our objectives is to hire primarily honors graduates. Now, when we set that objective, we have to recognize that we will lose probably more of those than if we hired the run-of-the mill examiners.

But our major objective in the Patent Office is to issue quality patents. I do not want any junk going out that front door, and the honors graduates is one element that we are going for in our attempt to reach that quality objective.

Chairman WYDEN. I have only one other question for my first round and will have some more in a moment.

Why are these problems, Mr. Quigg, of particular importance to the small companies? It seems to me there are at least a couple of problems. One, it is very serious when their financing is left up in the air. Second, it seems to me, they are not in a position to do the search that large companies can do when they are out looking at potential competitors.

There may be other problems associated with this process for the small companies, but tell us, based on your experience, why you think this is a problem, particularly for the small companies.

Mr. QUIGG. Well, I think it is a problem for the small company because, as you stated earlier, they need to go out and get financing to back them in their commercialization, and to a large extent, entrepreneurs are not going to move until they know exactly what sort of protection the company has.

Chairman WYDEN. In the granting of a patent, though, to some extent, your people do the search. So that when your people do it, the small company can be assured not only that they are going to get the patent, but that some of the groundwork is done.

The large companies, as we understand it, are in a position with their own resources to do some of the search in terms of where their competitors stand. It would seem to me this is another significant problem that the backlog causes for the small companies that the large companies do not have to worry about.

Mr. QUIGG. Mr. Chairman, I would say that I would disagree with that, because we have a whole search room of public searchers over there who are doing searches for people out of town, large-, small-, medium-sized companies.

Chairman WYDEN. But that is hard to understand, given the fact that your own people have told us it takes more than 2 years to open an applicant's file.

Mr. QUIGG. I am sorry. I do not get the connection.

Chairman WYDEN. Well, your own people have told us that it takes more than 2 years to open an applicant's file.

Mr. QUIGG. If it goes through the normal procedures, but if they file a petition to make special, it does not go through that.

Chairman WYDEN. We will examine the special procedures later, and I just again must state that I think people who run small companies are pretty interested in getting the earliest possible approval, and they are not passing up this expedited procedure for nothing. They do not seem to think it is the tool that you describe it as being this morning, and we will ask them some more questions about that.

Mr. TEGTMEYER. I would like to add that under the special procedure, if they file a request to have their application taken up out of turn, we will take the case up ahead of the other cases. Again, the normal pendency to the first action in a biotechnology area, we would estimate is around the 14- to 15-month area. Cases made special should be taken up within just a few months after the filing date, if the petition is filed early in the case.

Chairman WYDEN. Well, we understand that is the way the process is supposed to work, and for some reason, the small companies, literally thousands of them, are not using it. So, we are going to dig into this in some detail very shortly.

Let me recognize my colleague, and I will have some additional questions in a moment.

Mr. PRICE. Thank you, Mr. Chairman.

Mr. Quigg, I want to thank you for your testimony and would like to take up a couple of matters that are dealt with toward the end of your statement.

You state that you are predisposed against such options as the splitting of filing and examination fees or the use of internal priority documents. You do, however, say that you are not opposed completely to all innovations of this sort, and you are willing to consider some of the procedures that have been adopted in the European Community and Japan.

To deal first with the question of the split fees, what is the practice in Europe and Japan in that regard?

Mr. TEGTMEYER. If I can interject, Mr. Price. The European Patent Office, which handles patent applications that may become effective as patents in a large number of the Western European countries, does have a procedure whereby you pay a separate fee and file a separate request for examination.

However, when you pay, you must pay that fee within 6 months after the publication of your application, which occurs 18 months after filing, and I believe about 90 percent or so of the applicants do pay that fee and request examination. The procedure does not have much potential for reducing the number of cases that have to be examined there. In fact, we feel that such a procedure might actually, if you can file more cheaply, stimulate some increased filings, though not necessarily subsequently requesting examination for those particular filings.

I might also note that the separate procedures in the European Patent Office for search and examination are under review there, and they are giving serious consideration to joining the procedures together. That does not mean that you will not have to file a separate request for examination and pay a separate fee for it.

But since they are considering joining the procedures together, there does not also appear to be any efficiencies in their present separate procedures. They certainly have not realized any efficien-

cies by first conducting a search, completing that, and then entertaining a request for examination, and then conducting the examination where it is requested.

Their view is that is not the most efficient and effective way to operate anymore.

Mr. PRICE. And the Japanese practice?

Mr. TEGTMEYER. The Japanese practice also splits examination up, and you must file a separate request for examination, except that in Japan, you have a much longer period of time that you can let your application sit before the request for examination is made. In the mean time, of course, you get no examination nor does the rest of the public become aware of the patent rights you are going to obtain, unless and until you request the examination, and it is, in fact, completed.

Mr. PRICE. Might it not be the case, though, that in this biotechnology area, there might be a substantial number of cases where the applicant has no interest in an immediate examination, but, yet, would be served well by an early filing, and also by a split fee, especially a reduced fee, at the front end of the process?

Mr. QUIGG. Mr. Price, under our present system, I do not think there is that much to be gained by having an early filing and then doing nothing further about it for a period of time.

The Japanese have built in a 7-year period in which you can file an application and keep it pending for that 7 years before you ask for an examination.

The Japanese also are in a situation which makes their system almost unworkable. The Diet limits them to 1,000 examiners. They receive approximately a quarter of a million applications a year, utility applications. They cannot possibly examine those applications with that number of examiners.

So, they are coming up with a proposal now where they expect to farm out, to contract out the searching facility in order to get the searches back to the examiners and let the system work a little better.

But what we have tried to do is to hire as many examiners as we can, train them as sharply as we possibly can, so that they do a quality examination.

Mr. TEGTMEYER. If I can add, Mr. Price, while we are awaiting a request for examination, the rest of the public, the competitors of that applicant and others, do not know what patent rights may come out of that, and they themselves are going to have some of their plans upset if they want to develop the same technology, and they do not know for a long time whether or not those patent rights may affect their own development work.

Mr. PRICE. The Japanese, though, have more stringent publication requirements. Is it not true that Japan automatically publishes those patent applications 18 months from the first filing? Is there not a more stringent information requirement of that kind?

Mr. QUIGG. There is a provision for publishing 18 months after the filing. There is also the same provision in Europe, and I might point out that we are working very hard in trying to get some harmonization of laws worldwide.

The publication at the end of 18 months is one of the elements that we will be using as a trading tool in that harmonization proc-

ess. We are actually trying to get the foreign countries to go into broader coverage of technology, so that all of the inventions that might be made by our people here would be protectable in those other countries.

Some of the things that we have been talking about are trading materials, which we are using in our negotiation with the Japanese and the European Patent Office.

Mr. PRICE. So, you would acknowledge that those disparate publication requirements do put our country potentially at a disadvantage since the United States keeps these applications secret while the Japanese counterpart application is published at a much earlier date?

Mr. QUIGG. Well, let me tell you the problem with that. The 18-month publication is a document which is a disclosure, but you do not know what actual protection is going to come out of that application.

In our country, we are striving our level best to get to a point where the actual issuance of the patent along with the claims takes place within that 18-month period.

Mr. PRICE. All right. So, you really have serious questions about the 18-month publication requirement. You have no use for the idea of a split fee. You do not like the idea of internal priority documents.

Yet, you say here that there might be some ideas that the Europeans and the Japanese are using which would offer certain advantages in the United States.

What are you talking about, if these ideas have so little appeal?

Mr. QUIGG. Well, those ideas are simply a part of some 16 or 18 points that we are using in the exchange of give and take on the harmonization matter.

I would say that I would put our system up against any one of the systems. I do not care where it is. I think as far as quality patents are concerned, we are giving our applicants here a better patent than they can get in the other countries.

Mr. PRICE. Now, you do acknowledge that your own expedited procedures are not being fully utilized.

Mr. QUIGG. Yes.

Mr. PRICE. You expressed some puzzlement at that fact.

I understand that those expedited procedures do contain certain complexities. Let me just talk with you a minute about that.

The petition to make special. My understanding is that does involve the payment of a $72 petition fee. It involves, second, the applicant himself searching the case and reporting the findings of the search to the examiner. It involves, third, the applicant himself providing a legal argument concerning the patentability, instead of the examiner first giving his opinion. Finally, it involves the waiver of certain procedural rights during prosecution.

Now, my question is, first of all, are those conditions accurately stated? And, then, second, might these conditions help us understand why these expedited procedures are not fully, or frequently, utilized?

Mr. QUIGG. Well, I think, essentially, your summary of the requirements is correct. I do not see those requirements as being real

impediments for an organization that wishes to get an early issuance of a patent.

As I pointed out before, there are public searchers over there who are fully capable of making a search for the potential applicant if that is desired.

The requirements of making the arguments over the references is something that we require in all instances of attorneys who are prosecuting applications before the office.

So, there is no real difference there. The distinction must be argued when the references are cited.

Mr. TEGTMEYER. If I might add, Mr. Price, the applicants frequently, most often, are in the position where they know the area of technology that is covered by that application very well, and they know a lot of background information in regard to that application that will help the examiner tremendously if it is provided to the examiner. They know the field. They know how to do the search or certainly can work with a private searcher who can conduct a search for them, and provide our examiners with a lot of very good information that either the examiner may have a lot more difficulty finding or that may be pulled together much better because they know the technology better than the examiner.

We can get a much better quality examination if the results of their background information and searches are provided to the examiner.

Mr. PRICE. So, your position is that these requirements for the expedited procedures are not particularly onerous, and that they do not constitute a very convincing explanation for these procedures being so infrequently used? That is your position?

Mr. QUIGG. That's my position. I would also say that if there is difficulty, we stand ready to work with the individuals to help them expedite it along.

Mr. PRICE. Of course, that then returns us to Mr. Wyden's earlier question. What does explain the negligible use of these procedures, and is it your conclusion that the need for expedited procedures has been overstated?

Mr. QUIGG. No; I cannot say that the need for expedited procedures has been overstated. Neither can I get inside the head of the individual who is filing the application and know why he is not using it.

The fact is that they are not using it.

Mr. PRICE. Well, perhaps our next panel can shed some light on that.

Thank you, Mr. Chairman.

Chairman WYDEN. Let me again try to put my finger on this expedited issue.

Are you saying that the patent community and their lawyers are just not smart enough to do what you suggest?

Mr. QUIGG. Mr. Chairman, I do not know whether it is a matter of being smart enough or whether they do not want to. As I said, I cannot get inside the heads of those individuals to find out why they are not doing it.

The procedures are available, and the procedures are not being used.

Chairman WYDEN. Let me go back to this question of the dates and how serious the backlog is because I find it hard to follow some of the numbers that you all have offered up.

Now, in response to one of the questions I asked initially, Mr. Tegtmeyer indicated that it was correct to say the first action on a number of applications filed in early 1986 was just very recent.

Now, on top of that, the subcommittee has been told that it takes something like 2 years more to go through the actual award process, to be either told yes or no.

So, my calculations are that it is something over 4 years to go through the process, and, yet, you all have indicated that the patent pendency average is close to an 18-month period.

Maybe you could just set us straight on that.

Mr. QUIGG. The patent pendency average at the end of February was 20.4 months.

Chairman WYDEN. For biotechnology?

Mr. QUIGG. For the entire technology in the office.

Chairman WYDEN. What was it for biotechnology?

Mr. TEGTMEYER. In the biotechnology area, including all of the areas that now constitute the new group 180, which includes the three art units you have referred to earlier and former group 120, former in respect to these art units, plus another half of an art unit, in 120, that also handles some biotechnology and is being moved into 180, and in addition, the other three groups that are contributing examiners and applications to the new group 180, our best estimate, and we will know when the reports start coming in since the group was just formed, of the total pendency from the filing date to the issuance of a patent or abandonment of the application is somewhere around 29 months.

The average time of pendency from the filing date until the examiner first picks the case up for examination is probably something in the neighborhood of about 14 to 15 months.

The present pendency level in group 120 as it existed before the reorganization this week was 11½ months from the filing of the application until the first office action for the whole group, and I do not have a breakdown for the three biotechnology art units in that group. Our best guess is they are probably around 14 or 15 months also.

Chairman WYDEN. When all the cases are actually opened, will the pending average get better or worse?

Mr. TEGTMEYER. Go back to what I said before, which was if you want to look long range, look at what is going to happen to the pendency on a kind of steady-state basis. You would take the total number of applications that are pending, awaiting first action or about 7,000 cases. You take that and divide the examiner work output this year, or about 5,900 cases this year, and multiply that times 12, and you end up with something in the neighborhood of 14 months.

So, on the basis of a given inventory and the work flowing out of that inventory, the pendency would calculate out at 14 months. That means if you are on a perfectly steady state operation for a couple of years in a row, you put out the same amount of work and receive exactly that amount of work, then this calculation would work out to be your actual pendency level.

Chairman WYDEN. One last question on this averaging process. Does the average now include cases not yet open?

Mr. TEGTMEYER. The average pendency to first office action is a 3-month running average of the cases that actually get a first office action. That is how long those cases have been pending, on the average, when they get the first office action.

Some cases may be in the inventory, and there are cases in the inventory in the biotechnology area that are quite a bit above that. There are also cases in that inventory that are below it.

Chairman WYDEN. Well, it seems to me your answer is no to that question, and all I can tell you, Mr. Tegtmeyer, is my staff went down there, and we saw shopping carts full of these applications.

Now, we have gone through various ways to define what the pending period is, but what I see are the shopping carts. What we hear is from those small companies, ones that are really going to be at the frontier of progress in this country, who say they wait years and years and the problem is getting worse.

So, I think what I want to do now is go to your game plan to try to reduce the backlog and see if we can understand exactly what that is.

Mr. QUIGG. Mr. Chairman, if I might interject there. You are talking about seeing grocery carts full of applications with the checks attached. That is in the initial handling of cases and those cases are getting to the examining groups within 30 days, is it not?

Mr. TEGTMEYER. The goal is to get them to the groups within 30 days. There is existing now a backlog in the mailroom that receives new applications for the whole office, and it takes something a little less than 2 months to get the cases to the examining groups.

That has no effect, however, on the backlogs in group 120 because they are much further behind that date, and, so, speeding initial processing up would not reduce the backlog in group 120 or group 180.

Chairman WYDEN. So, you pick up the checks within 2 months, is that correct?

Mr. TEGTMEYER. The checks are picked up more quickly than that, but the cases are processed through the mail room and through an application division, which goes over the formal requirements to determine whether they have been met. We process the fees before it even goes into that.

We microfilm the case. We determine what technology is involved and what organization the case will be assigned to, and then it is put through a national security screening by examiners who come in from our security group, and then it is forwarded to the appropriate examining group that has responsibility for handling that case.

That whole process takes something a little less than 2 months. The mail room sorting itself right now is something in the neighborhood of 2 or 3 weeks, and that is when the fee is processed, essentially.

Chairman WYDEN. My staff saw applications in the distribution room just below receiving that were from 1986. I mean applications that had not even made the baby steps toward a decision, and my staff saw those during the tours.

I think what I would like to do now, though, is get to your plan to reduce the backlog, because Mr. Quigg has agreed with my conclusion that it is staggering by anybody's calculation, and the number one goal, according to the plan to reduce the backlog, and I quote here, "is to adjust the examiner complexity factor."

Could you, Mr. Quigg, tell us what the complexity factor is, and what your office has done in this regard?

Mr. QUIGG. Once again, I am going to defer to Mr. Tegtmeyer. They do weigh the complexity of the technology and determine how much time it should take an examiner to examine the case.

Mr. TEGTMEYER. We have a plan of approach, Mr. Wyden, to deal with several questions in regard to processing biotechnology applications. We are interested in assuring that the examination is a quality examination, as Commissioner Quigg indicated earlier, in addition to reducing the backlog.

Adjusting examiner complexity factors was for the purposes of giving the examiners handling certain technologies, certain parts of the biotechnology area relating to recombinant DNA and immuno assay technologies, more time to process the cases they are working on in view of the complexity of the examination process involving those cases.

That will have the effect of giving the examiner more time to handle the average application. If anything, that will have a bit of a negative effect on backlogs. We are addressing, as I said, both the quality issue and a backlog question.

Chairman WYDEN. So, according to the way you look at adjusting examiner complexity, it may add to backlog?

Mr. TEGTMEYER. That is correct.

Chairman WYDEN. I understand that you all desire to increase overtime as well to try to address the backlog problem.

How is this part of the program to work?

Mr. TEGTMEYER. Yes; we have been working overtime in group 120 and in all of the other examining groups very heavily since 1982, when we undertook the program to achieve an average 18-month pendency level throughout the office.

That has been worked in group 120, but not at the level that we think the potential exists for overtime. They have worked, in general, in group 120 considerably less overtime than most of the other patent examining groups. We feel the capability exists for increasing the amount of overtime worked in that group and including new group 180, as well.

What we want to do is stimulate more overtime among the examiners in that group in order to help address the backlog problem.

Chairman WYDEN. Well, our review of the Patent Office time sheets showed that there were not many people working overtime at this point. Several indicated to us that many of the biotechnology examiners either attend law school at your expense or have second jobs, which hinder overtime.

My question, given that, is how is more overtime a realistic way to really deal with backlog?

Mr. TEGTMEYER. We believe we can increase the amount of overtime being worked by the examiners in that area. That does not mean every examiner can increase the overtime level, but we feel

overall that we can increase the overtime level in that group. I am really speaking of new group 180.

Chairman WYDEN. I wanted to ask you about a couple of cases with respect to your people and their second jobs, and whether or not that may present a conflict with their employment at the Patent Office.

Now, we are informed of one recent case in which one of your examiners was recording overtime at the office but also working full time as a patent attorney in Alexandria, VA.

Are you all familiar with this case?

Mr. QUIGG. We are aware of one instance in which apparently an examiner was working for the office and, at the same time, was working for the law firm. When we found out about it, he worked for neither one of them.

Chairman WYDEN. Well, that is encouraging to know. So, you took disciplinary action, and the gentleman was terminated.

With respect to the new top official in the biotechnology department, I gather he is the gentleman who replaced Mr. Van Horn. Does he have side employment, and, if so, what is his side employment?

Mr. TEGTMEYER. He is right here. You may ask him. As far as I know, he has no side employment, except many after-hours in the Patent and Trademark Office, working for us.

Chairman WYDEN. Is that gentleman here and, if so, let us bring him forward?

Mr. QUIGG. This is Mr. Samih Zaharna.

Chairman WYDEN. We welcome you to the subcommittee, and why do you not come forward as well?

My question to you, sir, as the new top official in the department, do you have additional employment outside the Patent Office?

Mr. ZAHARNA. No, sir.

Chairman WYDEN. We appreciate knowing that.

Regarding the attrition rates, excluding the biotechnology area, group 120 appears quite favorable to the rest of the Patent Office.

According to the members of your staff, Mr. Quigg, much of this is because of its former manager, Mr. Charles Van Horn's professionalism and desire to maintain quality, regardless of push, to deal with the backlog.

What is your comment on your staff's observation with respect to Mr. Van Horn?

Mr. QUIGG. Well, I would say that each of our group directors is doing everything possible to obtain quality production.

I do not know that Mr. Van Horn's push is any greater than the other group directors. Quality is our number one factor, simply because if we issue a patent that is not valid, somebody is going to spend a pot full of money and get nothing for it, and we do not want a system of that sort.

Mr. TEGTMEYER. Mr. Wyden, I might mention when Mr. Zaharna first took the reins of the job he is in now, my deputy and I had very lengthy discussions with him in regard to the need to get rid of the backlog in group 120 and in new group 180, and the need to maintain a very high-quality examination in there. We discussed

this at great length, and he assured us that he is going to pursue both of those goals.

Chairman WYDEN. It is my understanding that more new examiners have been hired for other areas than biotechnology, particularly organic chemistry was one that our subcommittee was informed of.

My understanding is that there will be 45 new examiners over the next year, 25 for organic chemistry and 20 for biotechnology.

If biotechnology is so important and the backlog is so great, would not a sensible personnel practice mean that there would be more in the biotechnology field than in the organic chemistry area?

Mr. QUIGG. I would say that is not an accurate statement.

As I pointed out, we do not want to have examiners in there who are not properly trained. Unfortunately, we only have enough examiners to properly train 20 new examiners at this time. As the period moves on and additional examiners get experience, we would expect that number to increase to 25 and even a little higher than that.

But we have had a lot of experience in the office in the last 6 years. We have hired better than 1,100 new examiners in that period of time, three-fourths of whom have been honors graduates, but the only way we can do it is to have the people there who can train them so that when the new examiner gives an action, it is quality.

Now, the Grace Commission told us we could not train that many examiners. We have.

Chairman WYDEN. Well, not all of us go along with everything in the Grace Commission, and I guess it seems to me that you all have put out one of, I guess, the grounds to indict the present system, is that we are short examiners in the biotechnology area.

You make the point that we do not even have people to train those whom we would like to bring into the system, and it seems to me that is one of the central kind of failings. We need more people. We need more trainers, and, clearly, the number of applications is growing far faster than our resources.

Mr. QUIGG. Mr. Chairman, I would point out that this is a relatively new area, and not only are we looking for experience, but every law firm that I know of is looking for experienced attorneys also. They are having exactly the same problem that we are having.

Chairman WYDEN. Mr. Quigg, in your statement, you indicated the Patent Office has requested, and received, additional funds to hire more examiners since 1982, that your funding levels were adequate with the exception of 1986, to address any short falls in the examiner staff level.

Could you tell the subcommittee, for the period since 1982, how many examiners you hired officewide and how many were assigned to the biotechnology area?

Mr. QUIGG. Well, as I said, we have hired in excess of 1,100 new examiners in that time. I do not have the figure on biotechnology. Maybe Mr. Tegtmeyer has it.

Mr. TEGTMEYER. Since 1983, which is one year later than the 1,100 number for the whole corps, we have hired 74 examiners in the biotechnology areas.

Chairman WYDEN. How long will it take, gentlemen, to make significant progress in terms of turning around this backlog? Will it take till 1992 or 1994? When do you think we will have this problem under control?

Mr. QUIGG. Well, it will be completely under control by the 1993–94 period. That means that we will have brought the pendency down from 29 months that Mr. Tegtmeyer mentioned awhile ago, to 18 months.

Chairman WYDEN. What effect will this have on this promising new industry for America? If it takes until 1993 or 1994 to turn around this backlog, are we going to lose companies offshore? Are we going to lose jobs? What effect will this have?

Mr. QUIGG. I would say that with the special handling, the availability of petitions to make special, it should not have any particular effect.

Chairman WYDEN. Well, again, you basically are saying that the small companies and their lawyers are not smart enough to do what you are suggesting, and I must tell you that I think people with significant financial interest will take every reasonable step to secure those interests, and they are not using this procedure that, as you have told me and my colleague, Mr. Price, is so simple and so convenient.

We are going to hear from them shortly, but the proof is in the small number of applications that are going forward, and, for one reason or another, they are not using them.

Mr. QUIGG. I am afraid I do not know what the proof is.

Chairman WYDEN. The proof is the gigantic backlog, and only a handful have gone through this expedited process.

Mr. QUIGG. Those do not hang together. All I am saying is that the procedure is there, and if the attorneys will use it, they can get faster handling.

If they are having problems with it, I would say that we opened the door to have open communication with everybody who has problems. We have been doing that since 1981, when this administration came in, and if the attorneys do not feel that they can properly get the cases handled expeditiously, then they ought to come in and talk to us.

We have changed an awful lot of rules just to help the applicants get better handling of cases, and if this is a problem for them, then they ought to come in and talk to us about it.

Chairman WYDEN. I must tell you that I think there is a correlation between the huge backlog and the small number that have gone through this expedited process. It would seem to me that even a modest addition from the backlog would have gone the expedited route if it was as convenient and as accessible as you said.

We will go through that with them, and let me recognize my colleague for any additional questions he might have.

Mr. TEGTMEYER. Mr. Wyden, if I can just add something to what the Commissioner said in response to your question.

We did, in fact, meet with IBA people last week in regard to talking about the possibility of other criteria for having an application made special, and, as the Commissioner mentioned, we are open to the considering other criteria. We cannot, of course, handle all the applications special or none will get special treatment, but

there is no reason we could not, and we are open to the consideration of other criteria that will better satisfy the needs of the applicants, as the Commissioner already mentioned.

Chairman WYDEN. We are pleased to look at those new things, and I know of your meeting last week. I know that you set up this special unit that went into effect, I gather, yesterday. But it seems to me we are going to have to have a comprehensive approach to this and to just say it is going to take until 1993, as Mr. Quigg has talked about, does not seem to me to afford an appropriate Government response to what I think is one of the most promising industries for our future.

Mr. QUIGG. Mr. Chairman, one more point.

We are hiring as many examiners as we possibly can, but I am not sure that the point has been made here this morning that filings in this area are increasing at 12 percent per year.

So, we are struggling to keep our heads above the water or get above the water, and we are going to add the examiners as rapidly as we can to the extent that, when they are added, they will be properly trained and be able to be a positive addition to the office.

Chairman WYDEN. Let me ask one other question about the 1986 period.

In 1986, which you said was an especially difficult period for you, there were 10 examiners assigned to the biotechnology unit. Now, according to your staff, during that period, 12 examiners left the biotechnology unit.

Does that mean that there was a net loss that year of two?

Mr. TEGTMEYER. The number that I have is 10 hires and 5 losses. We hired 94 people throughout the whole Patent and Trademark Office. So, we gave the biotechnology area itself a relatively big chunk of the ninety-four hires that the Gramm-Rudman cuts allowed us to hire in 1986.

Chairman WYDEN. So, in 1986, which was the year of special difficulty, there was a net of five. There were 10 hires and 5 lost.

Mr. TEGTMEYER. That is correct, sir.

Chairman WYDEN. The only other question I had is why was Mr. Van Horn replaced?

Mr. QUIGG. He was replaced because we promoted him. We moved him to his position of deputy solicitor.

Chairman WYDEN. So, he was happy to have made the change in position?

Mr. QUIGG. Well, I would guess he would be happy going to the solicitor's office. It is a challenging job.

Chairman WYDEN. Was this a voluntary change ?

Mr. QUIGG. Yes.

Chairman WYDEN. Did he come to you about it?

Mr. QUIGG. No; we asked him to take the position.

Chairman WYDEN. Several members of your staff have said to us that in the new administration, quality is no longer to be considered the top factor. You have indicated to me today, and I appreciate it, that you are going to continue to emphasize quality.

Why would your staff be saying to the subcommittee that quality is no longer going to be as stressed as it once was?

Mr. QUIGG. Mr. Chairman, I spent 35½ years out in private industry getting patents for a large company, and quality was the

thing that was most bothersome. When I came into the office, that became one of my major goals.

Chairman WYDEN. I would like to question that answer, though. Several members of your staff have indicated that quality is not going to be stressed as it once was. Why would they be telling the subcommittee that sort of thing? Have any of you attempted——

Mr. QUIGG. Mr. Tegtmeyer has just reminded me of the fact that the complexity factor has been a major source of irritation with the examiners. That complexity factor was adjusted just a short time ago.

So, it may have been behind the statements that you got. I do not know.

Chairman WYDEN. I still cannot really follow that. Your people have told us that quality is not being stressed the way it should. They have volunteered that to us, and you are saying it has something to do with complexity and the complexity factor.

Mr. QUIGG. The complexity factor gives them more time to do their job. This goes to quality, and if they are saying that we are not paying attention to quality, they have not been listening, because we have put in all sorts of quality programs, one of which was initiated after a year of surveys and analysis surveys. We analyzed that, came up with 12 points that the examiners needed additional training on, and we have initiated our program to improve the examiners' training in those 12 areas.

Chairman WYDEN. Have any of your staff or your top assistants indicated that speed in getting through these backlog cases is more important right now than quality?

Mr. QUIGG. No, sir; in fact, we had to back off of the 18 by 1987, because (1) we had a budget cut, and (2) the filings were increasing sharply. The presentation that I made to Secretary Baldrige at that time was that we could pass applications out without paying much attention to quality, or we could go to quality and forget about the volumes, but my recommendation was that we try to maintain a balance between the two.

The Secretary considered it at great length, and he said that although he hated to back off of that 1987 target date, that he agreed with me that we should maintain a balance between quality and quantity, and to the best of my knowledge, and I am certain that the staff, my senior staff, has absolutely the same position, that that is the type of balance that we should and will maintain in the office.

Chairman WYDEN. Well, we wish to work with you, gentlemen. We know of shopping carts full of applications, some with checks that have been lingering around for what appear to me to be a substantial period of time, a backlog that Mr. Quigg has said was staggering. Mr. Tegtmeyer indicated to me that for several examiners now taking their first action on applications filed in early 1986, and, finally, we are told that things will not be turned around until 1993.

I am not convinced that we can afford to wait that long. I think we are going to be driving our companies offshore—the most innovative, most creative people in American industry—if that is the case. I wish to work with you. I think you have defined the two

goals, which are efficiency and quality, but a whole lot needs to be done to turn the situation around.

So, I want to recognize my colleague for any additional questions he might have.

Mr. PRICE. I have no further questions at this time, Mr. Chairman.

Thank you.

Chairman WYDEN. Gentlemen, unless you have anything to add, we will excuse you at this time.

Mr. QUIGG. Thank you.

Chairman WYDEN. Thank you all.

Our next panel, we will start with Ms. Linda Miller and Dr. George Rathmann. Let us call our other witnesses as well. Mr. Robert P. Merges, professor, Columbia University Law School; Dr. William Hostetler, director of technology and transfer, Oregon State University; Dr. Phillip Carter, director of biotechnology research at North Carolina State University; and Mr. Harold Wegner.

We will have all of you at the table, and we welcome all of you to our panel today.

We will make a copy of all of our witnesses' prepared remarks a part of the record in their entirety, and we will begin with you, Ms. Miller.

TESTIMONY OF LINDA I. MILLER, FIRST VICE PRESIDENT, PAINEWEBBER, INC.

Ms. MILLER. Thank you.

Good morning, Mr. Chairman, members of the subcommittee, and thank you for inviting me to address this important issue of the U.S. patent backlog and its effect on the growth of our domestic biotechnology industry.

In my testimony, I have attempted to establish three points.

First, the shareholders and financial markets consider patents, specifically patent uncertainty, as one of the greatest risk factors to investment in the biotechnology industry.

Among the wide variety of risks these entrepreneurial technology-driven firms face are patents and competition at the top of the list. The biotechnology industry to date has been heavily reliant on the public's willingness to invest in its future, so far to the tune of about $4 billion in the public equity markets and venture capital community.

This is an important source of financing for the growth of this industry in the future.

Second, because of the patent uncertainties that this industry faces, we are now, in my opinion, underinvesting in this important growth sector of our economy. As a result of the patent backlog, the biotechnology industry has a difficult time raising capital and financing its very competitive programs.

Without investments from the public markets, the entrepreneurial biotechnology industry is forced to sell its product rights and technology, the life blood of this future growth, to large companies with greater resources financially, including many foreign companies.

Third, companies spend resources inappropriately without U.S. patent protection and clarity. Why were there more than 20 interferon programs in the United States in 1985, where the patent situation in that program was clear? We see the same situation in many areas.

Wasted manpower, financial resources, and duplication of effort are the results of many patent delays.

Mr. Chairman, I thank you for convening this hearing to register our concerns with regard to the patent delays. I am hopeful that members of this panel and yourselves will find some appropriate suggestions to accelerate our consideration of patents and to provide that necessary protection for this growing and important industry.

I would be glad to answer any questions.

[Ms. Miller's statement, with attachments, may be found in the appendix.]

Chairman WYDEN. We will have some momentarily. Dr. Rathmann.

TESTIMONY OF DR. GEORGE B. RATHMANN, PRESIDENT AND CHIEF EXECUTIVE OFFICER, AMGEN, INC., THOUSAND OAKS, CA

Dr. RATHMANN. Thank you, Mr. Chairman.

Over a period of about 37 years in my industrial career, I have certainly gained a great respect for the patent system, and I believe it works, and I believe it works to stimulate innovation for the public good.

Amgen is a medium-sized or medium-large biotechnology company today, but we saw it all happen from the time there was only 1 employee to the time now where we have 360. Perhaps one of the most remarkable things about biotechnology is the speed with which things have happened.

We have been hearing about 18 months and periods up to 1993 and periods of this timeframe are foreign to biotechnology. We have raced ahead. In a period of less than 2 years, we moved from the first sense that we had a new molecule into extensive patient testing, but we did it with the quality that made possible safe treatment of patients over the past 2 years.

So, time is an unusual dimension, and I think it would be only natural that systems that have been in place for a long time are not used to the kind of time wrenching that we go through in biotechnology. We are competing on a worldwide basis and every day counts.

Now, Amgen is a company because of the expectations of investors that there would be patents to protect our new discoveries, and that is a big change from what large companies do. The patent system encourages the production of good products.

In the case of the patent system in biotechnology, it has created the industry to a large measure.

There is one other dimension I would like to mention, and that is that of the patients. I have a couple of tapes here, and if your subcommittee would like to view them later at your leisure, they take about 5 minutes to view the biotechnology industry through the eyes of patients today, and I think that you would see that the

patent system has stimulated some really wonderful things. I think in order for it to continue to do so, it has to try to keep pace with a revolutionary activity that is going on in biotechnology.

It is a difficult job, and we are most patient because we know the energies and efforts of these people are highly qualified, and they have worked very hard, and, yet, at the same time, time is terribly important for all of us.

Thank you.

[Mr. Rathmann's statement may be found in the appendix.]

Chairman WYDEN. Thank you, Dr. Rathmann. Professor Merges.

TESTIMONY OF ROBERT P. MERGES, JULIUS SILVER FELLOW IN LAW, SCIENCE AND TECHNOLOGY, COLUMBIA UNIVERSITY LAW SCHOOL

Mr. MERGES. First of all, I want to say I appreciate the opportunity to come and air my views, Representative Wyden.

Let me just quickly say a few things of an introductory nature.

First, I want to echo what Dr. Rathmann said. I come to praise the Patent Office, not to bury it; to criticize it perhaps a bit, but definitely not to bury it.

I believe in the patent system. In my scholarly studies of it, I continually discover new benefits. I think it is a wonderful institution, and I am here solely to try to help to make it better, rather than to criticize it in a deep way.

Second, patents have practical importance. In my practice experience as a lawyer in Palo Alto, I did work for a high-technology firm. We did a lot of licensing and venture capital startup work. One of the first things lawyers do when they look over a startup, is an intellectual property audit. We take a look to see what patents the startup firm has, what patent applications its employees may have filed, what kinds of trade secret protection they have as a program in the company. The lawyers try to get a full assessment of the intellectual property rights the firm is holding. This is because intellectual property is perhaps the most important asset a startup company has, rivaled only by the talents of the founders. Before a startup company has a product, a plant, or a market profile, it usually has an idea—often protected by a patent or patent application.

So, I can say that patents are extremely important. The standard operating procedure in the venture capital industry is to get an opinion letter, if you can, from an outside patent attorney. In fact, I have spoken with several patent attorneys in New York who do this on a regular basis. They have had to tell investors on a number of occasions that although the application on an important product was filed as many as 2 years before, there is no office action to report on yet. This leaves the investors in a state of significant uncertainty.

So, this is one significant impact of the backlog in biotechnology applications: It adds uncertainty at the financing stage of a startup company. If you compound that kind of uncertainty many times over, and extend it beyond the venture capital field into the licensing area, you will find the kind of uncertainty that we are talking about that is created by the backlog. I know the Patent Office has a top priority of quality, but at the same time, they have to realize

that at least that initial office action, some kind of indication to the attorneys in the case, is very important to investors and licensees.

Without some early indication of the status of the application, there is just nothing to go on, at least prior to the publication of any foreign patent application. It is extremely difficult to get an early read on whether or not you have really got something, and investors who are finance people, even though they hire technical consultants to evaluate the startup's technology, but until the firm has some indication of what the patent status of the invention, or the key invention, is, it really is working in a state of uncertainty.

I think it is important to realize that because of this uncertainty the patent backlog affects small firms more than large firms. Small firms rely on outside funding. They cannot internally fund risky projects. Small firms also rely on licensing deals much more than large firms do.

As an example, consider Genetics Institute, which has licensed Chugai Pharmaceuticals, a Japanese firm, to produce its erythropoetin [EPO] product. Without the outside distribution muscle of a larger firm like Chugai, small firms like Genetics Institute have a hard time distributing their products.

Licensing is so important in this industry that there are weekly newsletters devoted to announcing licensing deals and analyzing them. Stock analysts are also very aware of the importance of licensing—they scrutinize licensing deals very carefully. Licensing is one of the key ways that small companies are able to access the large distribution network that is necessary to get a product to market.

So, those are some of the problems caused by the backlog in biotechnology applications. Now, let us consider some possible solutions. Let me just turn quickly to a manpower training issue that I think is important. You will hear from the Patent Office that it is very difficult for the office to match the salary levels of outside industry, and while I do not want to concede that point totally, there is a certain amount of truth to that. There is just no way the office can match the salaries. The response should be to create creative and innovative nonsalary benefits for the examiners. For instance, step up the in-house training, if that is possible. Perhaps create an in-house master's degree program for people with bachelor's in related disciplines. Try to turn the attention of the senior examiners in a formal way toward training, perhaps by counting training time along with total patent application "disposals" when determining pay raises and promotions.

Right now, with the pressure on final disposition, that is with the pressure on all examiners, especially senior examiners, to pump patents out the door, my perception from talking to examiners and ex-examiners is that the senior examiners need to formalize the technical training given to junior examiners.

Now, the Patent Academy, which is an institution that all new examiners go through some time in the first year and a half of their employment, is an excellent training facility for the legal aspects of patent examiners' jobs. However, the technical training sometimes is shoved to the back.

I think innovative and creative solutions should be looked at by the Patent Office. I think they are an institution that is (a) very old and (b) partly because of that, particularly wedded to the standard operating procedures that they have used for years.

Again, I come to praise them and not to bury them. But I do think there is a certain amount of organizational innovation that is going to be required to beat the problem. For instance, instead of saying, it is the lawyer's fault that the petitions for specialness are not working, the office should ask what can we do to make them work? In order to increase training, for instance, they ought not to say we cannot match salaries. They should say, instead, how can we do it? There should be more of a can-do attitude rather than a cannot-do attitude, which I sometimes see from the office. I am an outsider, so maybe, it is easy for me to carp. Even so, these are things that I think anyone who has taken a few minutes to scrutinize the operations of the office might be able to come up with.

In terms of procedure and reforms, I would refer your attention to my written comments. I would like to emphasize one point from those comments: There is a way, I think, to link a solution to the backlog situation with a procedural reform in the office that will make our patent system more in harmony with those of the rest of the world. On this I will defer to my colleague, Harold Wegner, for a fuller oral description.

A total solution—quality, breaking the backlog, and institutional procedural reform—is going to be necessary to beat the problem, which I do think is a significant one.

I appreciate the chance to address it. Thank you.

[Mr. Merge's statement may be found in the appendix.]

Chairman WYDEN. Thank you for a very helpful presentation. Mr. Wegner.

TESTIMONY OF HAROLD C. WEGNER, ADJUNCT PROFESSOR OF LAW, GEORGETOWN UNIVERSITY, WASHINGTON, DC

Mr. WEGNER. Thank you very much, Mr. Chairman, and members of this subcommittee.

This subcommittee is to be very much congratulated for the constructive approach that you are taking to a problem that everyone on this panel realizes exists. Following up on what Professor Merges has said, I, first of all, agree completely with his positive approach.

I look at the problems slightly differently, but with the same result. I see three different problems and three different solutions that we can have.

First there is the preoccupation with bean counting. We have talked about pendency. Now, you and the Patent Office are both technically right. You are talking about taking years to get an action, and the Patent Office is talking about 14 months or 2 months. We are using different accounting systems. There was one clear, gross misstatement in the opening remarks in the first panel. It was said that there is an 18-month publication abroad. That is correct, 18 months from time zero. Zero being the date of first filing. The first application is published in Japan and Europe at that time.

The Commissioner said that we are reaching an 18-month goal in many parts of the office. That 18-month period is counted only from the last patent application in the series. In other words, there is an accounting gain. There is a refiling of cases. So, a first case could be pending for 15 years, then it's replaced by a second case pending for 6 months. The pendency of that case under the bean counting approach is 6 months. Forget the first one.

So, we are playing games here. We will never reach 20 months actual pendency from the first filing date. We will be lucky to reach 30 months.

Now, what does this bean counting do? We have created an electronics sweatshop for the patent examiner. Every time the examiner acts on a piece of paper, he fills out a computer form. The Patent Office knows exactly what his backlog is, and there is an inevitable problem of focusing upon the disposals, disposing of cases. Professor Merges has some constructive suggestions for can-do solutions. I think they are excellent.

We must break this electronics sweatshop mentality.

The second point is triage. We have 116,000 patent applications in all technologies being filed each year. Perhaps, in 90 percent of the cases, the applicant does not want an immediate examination. So, we could RIF, get rid of 200 or 300 examiners and still focus our attention on biotechnology.

We could serve the biotechnology community. Let us let the people who want their patent applications examined, have them examined, and those that do not, have them postponed.

The third area is patent simplification. We had the very best patent system in the world in 1836, and 1836 was the last time we made major wholesale changes to our system. Germany, Japan, France, Great Britain, and every other major country of Western Europe and Japan have made wholesale changes in their patent laws in the last generation.

Canada, just last year, has joined the 21st century and modernized its law. I do not necessarily disagree with Commissioner Quigg when he says that we should have some bargaining chips or trading tools. But, it is absolutely insane for us to say, here, we will not publish our cases for our own community, when the rest of the world publishes their cases. What kind of a trading tool is it to say here, I will put a gun to my head, and I will blow my head off, unless you harmonize with us? That does not make any sense.

And, again, I congratulate this committee on its constructive, positive approach. I think it is very necessary. I am particularly pleased to have heard Professor Merges' comments, which are very constructive and could lead to a better system.

Thank you.

[Mr. Wegner's statement may be found in the appendix.]

Chairman WYDEN. Thank you. Both of you are making the point that we are going to stay with this until we really do see these changes implemented. I will have some questions, as I know my colleague will in just a moment.

Dr. Hostetler, we take special pleasure in welcoming you for Oregonians. We will make sure you have good loud mikes so that all can hear you. Let us move those around to you. We take special

pleasure in your coming a long way to be with the subcommittee today.

TESTIMONY OF DR. WILLIAM HOSTETLER, DIRECTOR OF TECHNOLOGY TRANSFER, OREGON STATE UNIVERSITY, CORVALLIS, OR

Dr. HOSTETLER. Thank you, Mr. Chairman.

I am the technology transfer director at Oregon State University, and I would like to address this topic from the university's point of view.

I would like to address some of the problems that this delay causes the universities. First, the delay in receiving the first action can create problems for universities that are considering filing foreign patent applications.

In most foreign countries, applicants have 1 year from the date of the U.S. filing to receive the benefit of the U.S. filing date. This is important. The expense of foreign filings is very high, and universities are under tight budgets as are all Government agencies, and it is desirable to have the initial opinion of the patent examiner before deciding whether or not to file in the foreign countries.

This means you have to have that first action prior to 1 year, probably in 9 months would be better, so that you can file that patent application.

With the slow response time in the biotechnology area, we are talking 28 months for that first action. Universities often commit substantial funds on foreign patent filings before receiving information from the U.S. Patent Office that protection is unlikely.

Second, universities, especially public institutions, have historically required researchers to publish. The number and quality of publications weigh heavily on the tenure and promotion process. State right-to-know laws make it difficult for State institutions to maintain trade secrets.

In many instances, enabling publications concerning a patentable technology is in print very soon after a patent application has been filed. In many cases, even before that application is filed.

There have been instances of companies having marketable products on sale based on information derived from academic researcher publications long before the institution has received the first action from the Patent Office.

Third, many of the examiners in the biotechnology field are inexperienced and tend to cite prior art and technical objections in their first office action, rather than addressing the issue of patentability and the merits of the claim of the patent.

Fourth, the cost of receiving patent protection is a major concern to universities, most of which utilize private patenting firms. The cost of receiving a U.S. patent application in most fields runs between $3,000 to $6,000. However, in biotechnology patents, which are more difficult, the costs are between $8,000 and $15,000. This cost differential is primarily due to attorneys' fees and the time factor involved in responding to the technicalities and, in a sense, educating the examiners concerning the specific biotechnology and how it is different from the existing biotechnology.

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Oregon State University has roughly $80 million worth of research each year. We received 40 patent disclosures from our inventors last year. This is a very small number of disclosures, but if you took those 40 disclosures and applied for 40 patents, which we did not do, we only applied for 6 patents last year, because of the cost factor, however, if you applied for those 40 patents, and you take the $6,000 figure on a regular patent, you are talking a quarter of a million dollars in patent costs.

Most universities do not have budgets that allow that kind of spending in the patent process. Therefore, many patentable technologies that could come from the basic research conducted by universities are not brought forward. We have to let the ideas die or publish because we cannot afford to take all the ideas that come forward and go for it.

Another problem for the universities is that the researcher whose primary duties are to educate students and conduct research, is the person who, if he or she discloses a new invention, must spend a great deal of time responding to the patent attorney who, in turn, spends time and money educating the examiner.

Many researchers are involved in new research before we receive a first action from the Patent Office and are hesitant to spend a great deal of their time explaining research that occurred 2½ or 3 years ago. This creates an atmosphere where many researchers are hesitant to bring their ideas forward.

Perhaps, it would be beneficial to have examiners visit industries or universities in the education process. If they have a greater understanding of what was happening in our laboratories or in our research offices, it might speed up the patenting process.

Concerning the Patent Office specifically, I have two points that were brought forward by the six different attorney firms we use in filing our patent applications. First is the idea of making applications special.

It has been suggested that if an inventor desires to speed up the patent process, he can file an application to make special. When you file an application to make special, they put a tab on your application, and it takes precedence over all other applications that are not marked to receive special attention.

Why do not universities take advantage of this? Well, it is not because we are not aware of it. Our attorneys are fairly intelligent gentlemen and ladies.

This classification was originally set up for patent applications that were to be involved in infringement cases. It has been modified since then, but there is still a feeling that if you apply for special consideration, your patent may be received sooner, but it is going to be subjected to extra scrutiny by the examiner, who is being more cautious knowing that there is an extreme likelihood of the patent being considered as an infringement case.

Another factor why universities have not used this process is the cost. To apply to make special, you have attorneys that have to do a search. They have to give a full patentability analysis and that attorney is basically spending a great deal of time and effort.

You are talking between $1,500 and $2,000 for this opinion. When you add this cost to the already higher cost of the biotech-

nology patents for a small company or for an institution, it is a cost that basically we just cannot justify.

Obviously, if we have special cases that come along, we may move them ahead, but using application to make special does not solve the backlog problem. If everybody used it to make their applications special, you have still got the backlog.

The second issue that the attorneys brought up is that the patent examiners in the biotechnology area have unwritten standards that they are utilizing, and our attorneys feel that if these standards were formalized and shared with the attorneys that are creating the applications, we could create better applications which would move faster through the process. If we are both working on the same wave length, have the same goals and objectives to work with, patents would take less time in the process, we would have less actions, and you would speed up the whole process.

We feel very strongly that there is not only an education process needed for the examiners, but also an education process for the attorneys by letting them know what the examiners want, what they are looking for, and if their criteria are changing. Let us know those changes and criteria so we can create better applications and speed up the process.

In closing, I have a few suggestions that I feel might speed up the process of the Patent Office. First, increase the time allowed for an examiner to spend on a specific case. Right now, there is a quota system. You have to get a case out within a certain time from the time you pick it up. It does not matter whether the case has 23 claims or 122 claims. You have a specific timeframe to work in.

If an application has 122 claims, it will take more time to review it and understand it than an application with 10 or 15 claims. Encourage the examiners to go to the substance of the application rather than the formalities and citing technicalities in the first action.

In many cases, in the first action, the examiner has not read the claims. They don't understand the claims. They pounce on technicalities. They kick it back out and say respond to these, but they do not know what is going on, and, so, you are still in that educational process.

Second, provide the examiners with adequate support staff. You talk about plenty of shopping carts and this kind of thing. Well, it does not take an examiner to do the busy work like photocopying. You do not want an examiner to do this kind of thing, so give them the support staff to get these cases moved along. Get the process cleaned up for them so that they can spend their time working—looking at applications and making decisions on patentability.

Be consistent on the kinds of claims allowed and standardized criteria for the claim scope. That will enable patent attorneys to prepare applications that should move more swiftly through the process, thus decreasing the backlog.

Each case in the biotechnology field is highly specialized. No two cases are going to be exactly alike. It is not like working in electronics where everything works on a certain series and this kind of process. It might be beneficial to have the examiners be encour-

aged to discuss the technology with the inventors early in the application process.

As was mentioned during the first panel, the inventors are the ones who know what is going on. They have the basic understanding. So, have the inventors and the examiners get together early in the process to get an understanding of the invention.

As I said before, encourage the examiners, as part of their educational process, to visit industry or research laboratories as an educational tool. We need to spend some time getting these people up to par on what this technology is. We cannot expect them to know what is happening in the laboratories unless they have seen some laboratories operate.

Examiners in the biotechnology field must be highly knowledgeable individuals. Their skills are in demand. To hire and maintain these individuals, the salary benefits, the support staff, and other working conditions must be competitive, and this cannot be, I do not think, over-stated. You have to pay more to get an experienced person in the biotechnology field.

Thank you, Mr. Chairman.

[Dr. Hostetler's statement may be found in the appendix.]

Chairman WYDEN. Thank you for an excellent presentation, Doctor. I think you make the case very well that we really have a quill pen system to deal with the 21st century technology, and you give us very good suggestions. I will have some questions in a moment.

Dr. Carter, we welcome you to the subcommittee. My colleague, Mr. Price, knows of your expertise more directly than I, but we welcome an individual of your stature in the biotechnology community and look forward to your statement.

TESTIMONY OF DR. PHILIP CARTER, DIRECTOR OF BIOTECHNOLOGY, NORTH CAROLINA STATE UNIVERSITY, RALEIGH, NC

Dr. CARTER. Thank you very much, Mr. Chairman, for giving me the opportunity to testify before the subcommittee this morning on the perspective from a research university.

My statement this morning is a condensation of a white paper which I have prepared for the subcommittee's use, which I would like permission to append to this testimony.

The hearing today is to address the question of whether there is a problem with the estimated 4½-year backlog in the issuance of patents in the field of biotechnology. The answer is yes; there clearly is a problem and one that needs attention.

The patent statute requires the Patent and Trademark Office to keep pending applications secret. Therefore, the longer a patent takes to issue, in any field, the greater the chance of another patent claim issuing which takes precedence.

In an area such as biotechnology, with the quick-moving developments that occur in such a field, any backlog results in concealment of unknown art and deprives the public of any idea as to the breadth of such unknown art.

Second, it withholds important technology from the public. An example is TPA, which has been developed to dissolve blood clots. The time spent in studying the patentability of such an invention

increases the time lag between discovery and commercialization, and time and research effort lost because of confusion over patent status.

Third, the long backlog in time from application to issuance severely inhibits the public's desire to invest in an invention. The first patent that issues affects how people invest their research dollars. People invest on the basis of what patents are issued. The patent backlog always impacts on how research dollars are put in.

Universities are particularly hurt by the long backlog because we have comparatively little money to gamble on a patent application by a faculty member who may have a promising invention. We do not know whether the biotechnology invention will be preempted by a patent which has been filed several months or many years prior to our filing.

Since patent applications are secret until they issue, this prior art is hidden from the university until issuance and until that time, the university has no idea as to the area of the patent or its breadth, either of which could block the patent we have under consideration.

Backlog is, indeed, a problem. The goal for the Patent Office in the area of biotechnology should be twofold. First, the patent application should go to review within a 10-month period. Second, the patent should issue within 2 years.

Some solutions have already been proposed. These are good solutions, but do not fairly address the backlog problem. One solution proposed is the development of an internal priority document [IPD]. The IPD has the effect of being a patent application and could be relied upon to establish a date of invention under the international convention on patents.

Other countries allow the IPD to take the place of the full patent application, even though it is a much shorter document. It does not fully describe the claim. This addresses the problem of speed, but encourages broad applications. Broad applications, in turn, would diminish the ability of the small investor, or small inventor, of participating in the development of a particular area of technology.

The second proposed solution is to split the filing fee from the examination fee. Splitting the examination fee allows those in a hurry to have their claims examined first by paying a larger fee. Splitting the examination fee from the filing fee, however, favors deep pocket investors or large corporations and does not help the university researcher or small companies in developing new areas of technology. Splitting the fee does not lessen the current backlog.

A third proposal is to go to a first to file situation which is common in countries other than the United States. This may be acceptable. But if the first to file proposal would do away with the 1-year grace period in filing a patent claim, which the United States currently recognizes, it would be a disaster for universities and small businesses.

Current law permits us to discuss freely any new invention and gives a 1-year grace period from the time of publication, whether it be in writing or verbally, such as at a research meeting, and the time of filing. The university environment is one in which publication is encouraged and in which free exchange of information is commonplace.

It would be very difficult to establish a first to file situation without a 1-year grace period given the free exchange of information present in the United States.

The current statutory 1-year grace period contributes to the ability of any inventor in this country to work on an invention and determine its economic potential prior to investing large sums of money in a patent application.

I would like to propose some solutions which would be acceptable to research universities and, I believe, small business. These possible solutions would directly address the problem of backlog and unacceptable delays in the issuance of biotechnology patents.

The Patent and Trademark Office is already reorganized to address the backlog by creating a biotechnology expertise group, having taken examiners from related fields and moved them into a group which would examine biotechnology patents.

Certainly, the Patent and Trademark Office is to be commended for moving expeditiously in this regard. However, it is only a Band-aid and more changes are needed. Increased compensation to retain experienced examiners is necessary.

Within the Patent and Trademark Office, especially in areas of biotechnology, examiners are often recruited by corporations developing inventions in this new field. The Patent and Trademark Office finds itself, as it often has, in direct competition with universities, corporations, and small businesses which are also trying to recruit talent in biotechnology coming out of Ph.D. programs, university Ph.D. programs, and postdoctoral programs.

It may be possible upon further examination of needs in the area of biotechnology patents to reduce the qualifications of the majority of the staff needed to examine patents in biotechnology. Although there are a fair number of Ph.D. examiners in the other arts, the tendency has been to try to recruit only Ph.D. level examiners in biotechnology.

My university and many others in this country have excellent programs in areas of biotechnology, and I feel that our bachelor's and master's degree students coming from these programs may be able to fill the openings in the Patent and Trademark Office in the area of biotechnology.

Another proposal would be to develop additional information sources available to the examiners, permitting them to expeditiously research the literature. Biotechnology is such a new field that prior art is mainly found in research publications and not in prior patent applications.

Examiners need systems to allow them access to these sources of literature.

Finally, the industry and universities should recognize their responsibility to educate biotechnology examiners. We should develop programs which would allow patent examiners of biotechnology to actually visit the research laboratories of small and large companies and universities tc get a better feel for the emerging technology.

This is commonly done in the other arts, but is yet to be developed in biotechnology.

In my opinion then, these four solutions will improve the backlog. First, increase compensation to retain experienced examiners.

Second, reduce the qualifications acceptable for examiners. Third, increase information sources available to examiners to permit literature searches, and, fourth, develop field education programs for the examiners.

These solutions should help us achieve the goals of patent search and first review within 10 months and issuance within 2 years.

Thank you, Mr. Chairman.

[Dr. Carter's statement may be found in the appendix.]

Chairman WYDEN. Doctor, thank you, and I want to thank all of our panel for an excellent presentation.

I will have a number of questions in a moment, but I want to recognize my colleague from North Carolina to begin.

Mr. PRICE. Thank you, Mr. Chairman.

This has been a very enlightening panel discussion. I think if there was any doubt that we were on to a real problem, it would have been dispelled by the discussion that we have just heard.

It is frustrating to realize the kind of ways we have handicapped ourselves in this area by virtue of this backlog, these delays, these costs. I come from a State that has a tremendous stake in biotechnology. We have invested as a State government in the North Carolina Biotechnology Center. We have over 100 biotechnology firms, have outstanding research universities, and what we have learned today is, I think, something we need to attend to.

We have subjected these universities and these firms to costs, delays, and uncertainty about their investment and research decisions. It is clearly a problem that we need to resolve.

I have a few questions which have to do with some of the specific remedies suggested by the panel, and some differences, I think, among the panel members. I may not be able to discuss all of these, but I would like to explore some of them.

You seem to have somewhat different views about the practicality and the desirability of some kind of internal priority document system.

Dr. Carter is somewhat critical of the IPD system. However, the rest of you seem to be somewhat more favorably inclined.

Would one of you wish to elaborate on that suggestion?

Mr. WEGNER. Thank you, Mr. Price.

I do not think the internal priority document need be for everyone, but I think it should be available. The Germans, everyone in Europe, and the Japanese have this available.

In the mechanical arts, a German can file what is called a Gebrauchsmuster, a utility model case, for about $30. He can stamp in his invention, and he gets a filing date. He has 1 year to fix the case up, replace it, and make a more formal case.

Now, this is related to the grace period, and I am glad that you brought this up, the grace period. Every time that a U.S. inventor relies upon the grace period to establish a patent right, every time, he has forfeited all of his foreign rights.

As a public policy matter, this is scandalous. It is atrocious. In other words, every time that we publish first, every time we publish in a scientific journal, before we file a U.S. case, we have forfeited absolutely our European patent rights, and with a very narrow exception, our Japanese rights have been highly prejudiced. There is a limited 6-month grace period in Japan.

I do favor retention of the grace period. Nobody here has suggested that the grace period be done away with. If anything, we are trying to export the grace period to other countries. But the internal priority document should be a very simple system where I take my invention disclosure about to be sent to *Chemical Engineering News* or *Nature* and I, boom, stamp it in, pay $25, and that case sits in the Patent Office for 1 year, and then I can replace it.

Now, I do not say that the gentleman from North Carolina must use it. He should not be forced to use it. If he is not interested in protecting his rights in Europe and Japan, he should not be forced to use that. He should be able to rely on the grace period.

But in the biotechnology areas, I think when you have a $50 million cost to develop a drug, you have got to spread those costs worldwide. Otherwise, for one particular biowidget ultimately commercialized, you have 50 or more different chemical entities or biochemical entities that are candidates. The one that you are going to commercialize will be the one where you can spread those costs to all three territories—Europe, Japan, and the United States.

That is why an IPD to me is essential. We must provide this as an option, particularly for the small inventor.

Mr. PRICE. Do any of the panelists wish to comment on that proposal?

Mr. MERGES. I would like to say that I took the objection to be that the IPD would require the elimination of the grace period. Was that the substance of the objection?

Dr. CARTER. No, sir; I was very careful to state that if the first to file proposal was pursued, that we retain the grace period.

Mr. MERGES. I understand that. So, is your only objection——

Chairman WYDEN. Let us answer the gentleman's question, and we will probably want to see those in the field discuss some of these issues as well on another occasion.

Mr. MERGES. I am sorry.

Chairman WYDEN. The gentleman from North Carolina.

Mr. PRICE. No; go ahead, please elaborate.

Mr. MERGES. My answer was that I agree with Mr. Wegner, and I am not aware of any proposals that link the IPD to a dropping of the grace period. I would say from the university perspective, which is my perspective, the early disclosure and the sharing of scientific information that the grace period fosters is an important policy goal that the patent system has always advanced, and I support its continuation.

Mr. PRICE. Dr. Carter, would you like to expand on your reasoning?

Dr. CARTER. Yes; thank you, Mr. Price.

The grace period, as I have stated, and as my colleague from Oregon State has also stated, is very important to small businesses and to universities.

Certainly, Mr. Wegner's statement that the grace period is something we would like to export, and harmonization is something we would also support, because we think it is a good thing. We are very concerned about the first to file provision and being preempted in foreign markets.

However, the problem with the IPD is that it generates and facilitates broad applications, and this is a problem that is a very im-

portant one in biotechnology, and important to young industries; early broad patents actually stifle growth of small businesses in this area.

I can comment very directly. I am not an attorney, and I will not pursue any views on the first to file provisions, but I can comment as an immunologist. In fact, I am missing giving a lecture today to my students which, hopefully, when I give it on Thursday, will produce people who may very well be able to serve in the Patent and Trademark Office, and who will be able to recognize broad patents and obviousness in disclosure, both of which have been problems in the granting of early patents in biotechnology, and both of which have contributed, in fact, to stifling development by small companies in this country, those already established, and those which would like to be established.

Mr. PRICE. Yes, Mr. Wegner.

Mr. WEGNER. You are exactly right. If you can get on file quickly with an IPD or otherwise, you will get the broad patent. The early bird gets the worm.

I would rather have an American get the worm than a Japanese or a German because they have an IPD system now. They can get these early dates. So, we are living in a naive situation if we think that we can control the whole world's flow of applications.

The Japanese can file in Tokyo very simply and replace a year later. So, shall we permit the Japanese, as they can today, to file in Tokyo and then, 1 year later, under the international convention, get that early date for the United States? You are absolutely right that you will get broad patents if you can file early, and let us let the Americans get the broad patents just as the Japanese and Germans do today.

Mr. PRICE. But your point, Dr. Carter, is that this kind of broad application could put smaller firms, and more specialized firms, at a relative disadvantage?

Dr. CARTER. Certainly, your experience on this subcommittee, Mr. Price, would, I think, support that statement. The actual examples I could tick off my fingers, are not examples from foreign markets. They are American patents that have issued with very broad claims and, in some cases, would not pass the obviousness provision if, in fact, the examiners had the proper experience and training.

Mr. PRICE. All right. Let us move on to these expedited procedures, which the Patent Office supposedly is already attempting to implement.

Dr. Hostetler, I think, addressed that most directly, and cited some factors of cost and complexity that he thought had reduced the effectiveness of these procedures.

Do any of the rest of you have anything to add to that? Anything that we should consider in assessing the apparent ineffectiveness of the current expedited procedures?

Dr. RATHMANN. I am not sure that I can clarify too well, but two of our cases, we have requested they be expedited. So, we did not miss the boat completely.

I was looking in my mind here, thinking back, and in one of the cases, one of the most important ones, we filed in late 1983, and we did not request special treatment until some time in the summer of 1986, after the application had been going quite some time.

I cannot say I know all the answers. I am not an attorney. The reason that I understood that it took us that long was because we had the belief that there was the necessity to show some imminent issue with respect to competition.

That may have been, as I listen here today, the possibility of an older interpretation, and, maybe, we were not up to date, but we had some pretty good counsel. It was still my impression that it was only appropriate to ask for accelerated handling after there was some clear indication.

The fact, in other words, that we were a year ahead of everybody else would have suggested to us that we did not have a basis for asking for expedited handling, but because this field moves so rapidly, we realized 2 years later that we better ask for handling, or we would be on the market before we had our patent issued.

So, we did it. We have done it again in our latest molecule, and we do expect it to move more rapidly. In the first case, we asked for special handling in the summer of 1986, and the case issued in late 1987.

So, it does work. There is no question that it changed the priority, and I believe the system should be that way. I think we know which are our most important cases. We would not ask for expedited handling on all of them, and the only thing that I am understanding from what I heard today is we should fire it in there the day we apply instead of waiting for a year or two of disappointment and then go after it.

But we have done it, and it certainly helped.

Mr. PRICE. Good. Thank you.

Dr. Carter, a layman listening to this testimony today and to the account of this backlog and its effects, I think, could come to the conclusion that we are facing a substantial waste of creative energy and talent as scientists virtually reinventing the same wheel all over and over again or at least risk doing that, all because there seems to be no reliable record of who is doing what.

Is that really the situation we are facing?

Dr. CARTER. Well, it is a very serious situation, Mr. Price. The fact that these applications are secret until they issue creates, because of the backlog, a great deal of uncertainty among the investing public and, in fact, even among the research scientists who might be pursuing a development.

Mr. PRICE. So, you feel that this situation squanders our scientific expertise and significant capital? Is that fair to say?

Dr. CARTER. There is no question in my mind. The Science article which appeared at the end of February, which quoted or cited a 4½-year lag period, was probably being generous. Certainly, Genentech has been noted to have a very significant patent just issue after filing for it in 1977.

Mr. PRICE. This would seem to be a problem, not just from the scientists' and the investors' perspective in terms of delay, but it might also create major legal questions regarding the scope of the given patent and possible infringements on it.

Are we subjecting those seeking patents to legal problems and to possible legal conflicts?

Dr. CARTER. Certainly, the attorneys on this panel would support the statement that you do not have a patent unless, and until, it is

tested in the courts. We can file for a patent. The patent can issue, but we really do not know what we have until it has been tested.

In many cases, this has contributed to some of the problems in patenting biotechnological discoveries. The petition to make special, I think, is affected by this. Although the $72 filing fee, which you cited, is not exorbitant, you mentioned three other points that are required and costly. That is a search by the applicant, legal argument put together at the applicant's expense, and a waiver of procedural rights.

Friends of mine at IBM and Monsanto routinely make use of this sort of procedure, and I think that reflects the fact that it favors the deep pocket person because, although a $72 fee may be insignificant, the fees attached to these others, as has already been pointed out, are significant.

Now, if we look at each of those, the second and third points, from the perspective of biotechnology, there are still difficulties. A search by the applicant still creates the situation of convincing the examiner based on very little precedent that we are arguing from a point of strength.

A legal argument also carries very little weight without being tested to any extent in the courts. So, until we actually get patents issued in this field, it is going to be very difficult to fulfill points 2 and 3 by an applicant who may wish to take advantage of the petition to make special, but, as has also been pointed out by my colleagues on this panel, that does not address the backlog issue.

Mr. PRICE. Now, in your testimony, you deal with the delay that we are facing, but you also emphasize the question of quality, as did other witnesses.

Dr. Carter, in particular, you emphasized the highly technical nature of patent applications and the problem we have in giving a quality review to those applications. Is it fair to say you feel the major problem frustrating the application process is the lack of truly qualified examiners? How do the qualitative and quantitative factors interact in your view? Are there simply too few examiners or is there really a problem of qualification as well?

Dr. CARTER. I think the problem is twofold. As you have described, Mr. Price, that is, there are too few examiners and those people are not trained specifically in areas of biotechnology.

Biotechnology is moving very quickly and has moved very quickly. I spent 1978–79 in Oxford, working with Alan Williams, and Caesar Milstein at Cambridge, who subsequently got the Nobel Prize for development of monoclonal antibodies.

When I went over there, only very basic immunologists had any idea about monoclonal antibodies. When I came back to the United States, monoclonal antibody was the by-word. Today, not very many years after, the average man on the street can go into the drug store and buy diagnostic kits, such as pregnancy tests, that say on the box, monoclonal antibody. It is creeping into our everyday use.

That has occurred in a very short time. Shorter, in fact, than the universities can respond in training the many individuals in this area that are required by corporations, by universities, and by the Federal Government.

So, certainly, there is a problem with the number of people involved in this area to serve in the Patent and Trademark Office. The Patent and Trademark Office has responded by taking people in related fields and putting them into the biotechnology group. These people have some ancillary training in the area, but obviously it is not sufficient to make the judgments that are required of them.

Mr. PRICE. Do any of the other witnesses have some comment on this problem of training, recruitment, and quality? Yes, Mr. Wegner.

Mr. WEGNER. Yes; I can only echo very much what Dr. Carter and Professor Merges have said. I repeat again, we have an electronics sweatshop at the Patent Office, where numbers are everything. I repeat, everything. We are driving the good people out.

The one thing which should be added, it is true, the Commissioner's statement is true, that only a certain number of people can be trained, but that overlooks the fact that you could bring in top examiners at a senior level. Why not transfer senior examiners from less important technologies? There are also many people who are former examiners. They refuse to bring these former examiners back in because they come at a high level and it hurts the quota system.

They could be bringing in higher level former examiners, bring them back into the office, people in their forties or early fifties, and they could then train new examiners. So, there is more that could be done.

Mr. PRICE. Professor Merges.

Mr. MERGES. I was speaking with someone in the office prior to coming here today, and I asked about this problem, too, and I heard one anecdote I thought I might pass along.

The story was that one of the hiring officers in a biotechnology-related group wanted to hire two Ph.D.'s at a salary somewhat in excess of the normal starting salary of GS–10. The salary that they needed to offer in order to be marginally competitive was $32,000 a year to Ph.D. scientists, one of whom, at least, had significant postdoctoral experience.

The office denied the request for the extra funding. I think it is that kind of response that we need to pay attention to.

I also know of several people in my biotechnology seminar at Columbia and people a few years behind me in law school at Yale who are ex-examiners, Ph.D.'s with postdoctoral experience; the maximum time they spent as examiners was 1 year and 3 months, the average time a little less than a year. The reasons they left so soon were salary and working conditions. Standing in line to make photocopies, for example. A postdoctoral scientist coming from Cal Tech where he has three assistants to copy things, help with research, do whatever you want, goes to the Patent Office, has to wait in line four deep, and then somebody says, "Gee, it's not so bad today." That drives good people away.

Mr. PRICE. It must be bad if academic life looks luxurious by comparison!

I have presumed on your patience, Mr. Chairman.

Chairman WYDEN. Not at all, and we are glad you are here rather than pursuing academic life, I might add.

All of you have been very helpful, and I want to get a few things out on the record.

Mr. Wegner, you are a lawyer in private practice now.

Mr. WEGNER. That is correct.

Chairman WYDEN. You were in the examiners office for 4 years prior to going into private practice?

Mr. WEGNER. That is correct.

Chairman WYDEN. Now, am I to understand from your comments that you think the quality of work in the Patent Office is going down today?

Mr. WEGNER. I think it is very well documented. I would refer to published reports of Intellectual Property Owners, IPO, an organization which has consistently criticized the quality of the work product in the last few years.

In fairness to the present administration, this is a problem which goes back a long time, to at least 1963, when a commissioner of that era abolished the requirement for a law degree at certain high levels. About 1969, when other problems arose.

So, these are inherited problems to a large extent, and I think it is unfair to blame only the present administration. But, the quality certainly has gone down. We are paying lip service to quality in the Patent Office these days.

Chairman WYDEN. Well, my understanding is at one point you referred to it as junk in terms of the quality issue, and let me just state for the record that there is some junk going out in the main——

Mr. WEGNER. Yes; in the biotechnology arts. It is very expensive junk. I have to distinguish one statement that Dr. Carter made. He said that a patent is not valuable until it is litigated. In fact, if a big company has some of this "junk," it is a very powerful tool. The Federal circuit gives a presumption of validity to patents.

It is a very important piece of junk.

Chairman WYDEN. All right. So, we have established quality of work is going down, even though Mr. Quigg has said that is his top priority. We have established that some junk is going out.

I want to go next to this question of the numbers, because I really feel the basis of what I have been told today, that we are really seeing Patent Office cook the figures to some extent. They have cited this pendency period, I gather, of 19 months or thereabouts, but you have described to the subcommittee staff what you call the "Monty Hall Let's Make A Deal" school of patent application processing, and if I might summarize it, it seems to me what it consists of is, after things have gone on for quite some time, years, in a number of instances, what happens is they just refile it.

Mr. WEGNER. Coercively refile it. Not voluntarily refile it. Let me explain how that works. Let us say a case has been pending for 4 years, and then we are at a late stage in prosecution, after what is called a "final rejection." The examiner may tell the applicant, the good news is if you change the claims in a certain manner, I will allow the case. The bad news is it is too late procedurally in this case, so you have to replace this case with a new patent application. Then, I will allow your case.

So, then, the second case in the chain, or the third, or the fourth may be pending a total of 6 months. This is figured out at 6 months pendency for the invention, instead of the 4½ or 5 years.

Chairman WYDEN. I appreciate your insight into this, and I really do think that, to some extent, the office is cooking the figures in terms of what the period is, and I appreciate your enlightening us into the way the system really works.

One other question, if I might, for you, Mr. Wegner. I gather that you are concerned about this computer system that they are now implementing at this time. I gather it is called the APS computer system. It would cost hundreds of millions of dollars, and you feel this is going to make things worse?

Mr. WEGNER. In biotechnology, I think it is because it is increasing the cost. In the end, the patent applicants will pay for the costs, and biotechnology is a stepchild not benefiting from the system.

The computer system has originated without regard to biotechnology. In fact, the search text base, as it presently is constituted, is not usable for biotechnology. Now, they are trying to play catch-up and trying to fix it up, but the net result has been a negative instead of a positive. Plus it is costing the taxpayers a bundle.

Chairman WYDEN. How much of a bundle?

Mr. WEGNER. I am not exactly sure of the figure, but it is measured in terms of hundreds of millions of dollars.

Chairman WYDEN. We will ask the Patent Office on the record for that.

One other question, if I might, for you, Mr. Wegner, and then I have some questions for other panel members.

Could you tell us why the large major companies in the biotechnology field do not seem to be, in many instances, in a rush to get a patent and why it is the small business or the sole inventor really is hit by the backlogs?

Mr. WEGNER. Certainly. The large company, first of all, has its own top-level legal staff, and typically has its own corporate lawyers who are very well-trained in the particular biotechnology area. The company can then get its own opinion as to patentability without the need of some inexperienced examiner.

They also have their own search facility, but, more important, what I think Ms. Miller was pointing out before, is financing. The big company can let the invention sit and be developed whereas the small company needs that patent as part of its package.

I think Ms. Miller can address that much better than I can.

Chairman WYDEN. We are going to go on to Ms. Miller next. I understand on the basis of an analysis you have done, Ms. Miller, and you are with the firm of PaineWebber, that in the analysis you made of investor documents of the Securities and Exchange Commission, 93 percent of those documents indicated that patent problems, the black hole that we have described at the Patent Office, are what is discouraging biotechnology investments more than any other factor, is that correct?

Ms. MILLER. Yes; that is right. We looked at public offering documents from 44 companies that had been filed in 1986 and 1987. Thus, the concerns raised in these documents were relatively new ones. This is not reflecting ancient history. Looking at all the risk

factors, and there are about 40 different ones, depending on the company's business and its prospects, the two that jumped out most frequently were patents and competition. If you rank ordered them and weigh them in terms of the listing that they come up in, you still have patents in the top five as risk factors that any investor should consider before putting money behind the biotechnology enterprise.

Chairman WYDEN. Would it be fair to say that virtually the only time biotechnology stocks have suffered were as a result of patent uncertainties?

Ms. MILLER. I think that over time, biotechnology stock performance reflects a number of things—be it product development or the equity markets overall. Clearly, patents have had a negative and a prolonged negative influence on stock performance.

It is difficult to document that, but I think you can look at when patent situations clear up or clarify for companies, clearly, the stocks respond positively to that. So, I think the uncertainties do influence the stock and values of the company.

Chairman WYDEN. But you feel, first of all, the sector has great potential, and, second, the sector is threatened by the backlog that is now there at the Patent Office?

Ms. MILLER. Most definitely, yes.

Chairman WYDEN. I do not have any further questions that I wanted to ask. Actually, let me ask one other one.

Are there investors you know of who are passing on biotechnology, saying that, in effect, they want to go into other areas because there is no protection for their investment without a patent, and they see the patent process?

Ms. MILLER. Clearly, I think there are many investors, particularly individual investors, who view this as a very high-risk enterprise, and when they do not see that the efforts and struggles of these small companies to build businesses and address major problems that we have, especially in health care, they do not see any protection once that small company makes its developments and might even have to license them to a large company or an international company, they very often are willing to step aside and, in fact, might shift their investment strategy to those large companies instead of the smaller ones.

Chairman WYDEN. Or to simply go out of the country, shift the market, shift the job out of the United States, because domestic investors are not willing to take the chance.

Ms. MILLER. Yes; the alternative source of funds for many of these small companies, if they cannot go to the public in the United States, is to go to large corporations or, as you say, to go out of the country to get their financing sources.

Chairman WYDEN. It seems to me we are also wasting creativity, and, perhaps, Dr. Carter and Dr. Hostetler could address this as well. You have a situation because of this glut at the Patent Office and the investment uncertainty that you may have scientists all pursuing the same idea, without really knowing about it.

Dr. HOSTETLER. I can address that issue with an example. Prior to going to Oregon State University, I was at Washington State University, and we applied for a patent application on the sequencing of the recombinant bovine IL 2 gene. We filed that patent ap-

plication on May 13, 1986. We feel we were one of the first. We have heard that there were several applications now pending on IL 2 genes. Some not bovine, but the IL 2 gene.

We also were sure that there is a company in the State of Washington that has, since we sequenced the gene, also sequenced the IL 2 gene, and they are in the process of commercializing this technology, and they are moving ahead based on the fact that their people did it. We cannot license this technology. We have several small companies that expressed an interest in it.

The IL 2 gene is very important in working with several diseases, such as shipping fever in cattle, but these companies will not license and move ahead, when they have USDA approvals that have to be gone through, FDA approvals have to be gone through, and that is very expensive to a small company.

These companies say, well, we want it, but not until you know where you stand on the patent. To date, and this was patent application filed on May 13, 1986. Washington State University has not had an action.

Now, maybe we should have filed an application to make special, but we did not think at that time that it warranted that. We did not know we were going to have the 2-year delay when we first applied for this application. Hind sight is great, but when we applied, it was not a problem at that point in getting things out of the office.

Chairman WYDEN. I gather as well, Ms. Miller, that you think that the industry is still young enough to be particularly vulnerable to paper shuffling and bureaucracy at the Patent Office and will suffer as a result?

Ms. MILLER. Yes; I would agree. There are virtually no companies or less than a handful of companies that are profitable today in the biotechnology industry. Most of them, if you look at the amount of money they are putting into research and development, it is significantly in excess of their total revenue stream today.

So that it really is truly an investment that they are making in the future. They do not have the operating businesses that support those activities, unless they can count on the future and a lot of that will be protection of the products that they ultimately sell.

They are extremely vulnerable. So, I would agree, and I would say in terms of the timeframe of developments, it is an extraordinary situation within the industry. I think you see a lot of regulatory bureaus trying to speed up their review of these products, such as the FDA moving quickly on a number of these critical product development efforts, and it would be nice to see, once those products are commercialized, at least some patent protection for them.

Chairman WYDEN. One last question for you, Ms. Miller.

Do you think we can afford to wait till 1993 or thereabouts to turn this around?

Ms. MILLER. If I look at the development of the biotechnology industry, the first company in commercializing this technology founded in 1976 was Genentech. Within 10 years of its history and investment that it made, it has brought a number of major new medical products into common use, from the product we have all been hearing about, tissue plasminogen activator for heart attack vic-

tims, insulin for diabetics, human growth hormone, alpha interferon, and so on. It seems to me that in that short 10-year period, we have seen an incredible feat on the part of these entrepreneurial companies. To ask them to wait another 5 to 10 years before those property rights are protected does seem somewhat extreme.

Chairman WYDEN. Thank you, and you have been very helpful.

Dr. Hostetler, a couple of questions for you.

Does the current backlog of patent applications create a significant stumbling block for you and other researchers at Oregon State?

Dr. HOSTETLER. It creates the problem in the sense that there are several areas that I expressed earlier that it causes in the university setting.

Most researchers in the university setting are not wanting to go out and start up their own company. They are wanting to do basic research. They are proceeding ahead. They will make a discovery, and then they will go on and do something else, based on where their funding is coming from.

So, if you have a 2½-year backlog, you are asking that person to go back and respond to things that happened 2½ years ago, to go back and review notes from 2½ years ago, and they are interested in things that are currently happening, not the 2½-year ago problem, and their interest is really not in the receiving of a patent and the marketing of a product.

Their interest is the research. So, in that sense, the backlog is really hurting the university community. I go out to talk to these researchers. We encourage researchers to bring ideas forward. We do not force them to bring ideas forward.

So, we have to make that process as easy for the researchers as possible. So, yes; the backlog definitely causes a problem in the university setting.

Chairman WYDEN. Have there been lost opportunities for Oregon State in the research area because of these problems?

Dr. HOSTETLER. I can definitely say yes; there have been lost opportunities at Oregon State, but part of my initial process there is to talk to researchers and find out why they are not bringing their ideas forward. One of the main reasons they do bring ideas forward is the fact they just do not want to get involved. They want to do research, forget the patent process, it is too complicated and time consuming.

We try to make that process easier. That is why we have technology transfer offices at Oregon State, and that is why most major research institutions today have technology transfer offices, whether it is a foundation or an individual. Many universities have one single individual talking to about 1,500 researchers, and the duties of this individual include persuading the researchers to bring the ideas forward and then make that process easy for them, and a 4-year delay in applications does not make that process easier.

Chairman WYDEN. I gather that given the problem with the examiners, you and other people in the research community have to try to educate them as well.

Dr. HOSTETLER. Well, it all comes back again to the researcher whose main responsibilities are teaching and research, and that in-

dividual is the one who has to train our patent attorney who in turn responds to the examiner.

So, the patent attorney brings the questions forward, the researcher answers them, and then the patent attorney educates the patent examiner. It is a double education process. It all comes back to the researcher who really has little interest in whether or not a patent issues, other than possibly sharing in the royalties down the road.

Chairman WYDEN. At Oregon State, you all believe that established and uniform standards for patent application review would help significantly?

Dr. HOSTETLER. I think one of the ways of solving the backlog problem is the fact that if we know what the examiners need and where their interest is coming from, what kind of criteria they are using, our patent attorneys can create better applications.

I also feel that the State of Oregon and other States, such as North Carolina, are putting a lot of pressure on the universities to bring ideas forward. We need to make this process easy for the universities to bring them forward. We want to start small companies. We feel that is the backbone of the economy, yet it is hard for universities to work with small companies when we have such a backlog in patents.

Chairman WYDEN. I have no further questions for you, Dr. Hostetler.

I think all of you have been excellent witnesses. Suffice it to say we have an enormous job ahead of us. It is a job that is going to take resources. I think it is going to take a shakeup in terms of management decisionmaking, and it is going to be a major undertaking. But you all have made the job a little easier by giving us this helpful insight today, and unless you all have anything further to add, we will excuse you.

The subcommittee is adjourned.

[Whereupon, at 12:40 p.m., the subcommittee was adjourned, subject to the call of the Chair]

APPENDIX

STATEMENT OF DONALD J. QUIGG
ASSISTANT SECRETARY AND COMMISSIONER OF PATENTS AND TRADEMARKS
BEFORE THE
SUBCOMMITTEE ON REGULATION AND
BUSINESS OPPORTUNITIES
OF THE
COMMITTEE ON SMALL BUSINESS

U.S. HOUSE OF REPRESENTATIVES

MARCH 29, 1988

Mr. Chairman and Members of the Subcommittee:

I welcome this opportunity to testify before your Subcommittee on the operation of the Patent and Trademark Office, and specifically on our plans for handling the ever-increasing number of patent applications relating to biotechnology. Before, however, addressing the specific concerns expressed by you, Mr. Chairman, I would like to present a brief overview of the Patent and Trademark Office, its mission and its function.

Our patent system is almost as old as the nation itself. The first patent law was enacted in 1790, and this and later laws conferred upon the Patent and Trademark Office the authority to administer our patent system. This system has proved its worth time and again by providing the incentive to invent new technology, and to invest in its commercialization. Whole industries owe their existence to the availability of patents. In addition, an important source of technical information is provided to the

public and to industrial and scientific communities, permitting inventors to improve or to design around a competitor's patented products, thus bringing a steady flow of innovations to the market place. The availability of technical information through patents also permits the avoidance of costly duplication of research efforts.

The main functions of the Patent and Trademark Office are to administer the patent and trademark laws as they pertain to the granting of patents and the registration of trademarks. The Office has no jurisdiction over questions of patent or trademark infringement or their enforcement, nor of matters relating to the promotion or utilization of patents or inventions.

The examination of patent applications is the largest and one of the key functions of the Office. This work is divided among examining groups, each of which has jurisdiction over certain assigned chemical, mechanical or electrical technologies. At present, there are 16 examining groups, including one for exclusively handling patent applications relating to biotechnology that became operational just yesterday. Each group includes a number of suborganizations, called art units. Each art unit, so called because it is responsible for a specific area of technical art, is composed of examiners who review patent applications to decide whether the inventions described and claimed there are entitled to patent protection. On the average, there are 13 examiners per art unit and between 6 and 7 art units per examining group.

While there is a substantial number of administrators, lawyers, scientists and other professionals in the Office, the bulk of our

professional staff is made up of patent examiners. Our staff of 3,396 employees at the end of the last fiscal year included over 1,400 examiners. Each examiner handles patent applications directed to the field of technology in which he or she has been trained and is familiar.

The examining corps collectively examines applications in every technical field, ranging from relatively simple gadgets and toys to the newest developments in high polymer chemistry and solid state physics. The Office responds to the emergence of a new technology by shifting examining resources, within the examiners' capabilities and technical backgrounds, so that an invention in a new technology may be examined as promptly and thoroughly as other inventions in established technical disciplines. Our efforts to create an entirely new examining group for biotechnology is a case in point.

The patent examination process, of course, begins with the receipt of a patent application in the Office. The application is given a serial number and filing date by our mail room, and is then forwarded to an examining group for assignment to an examiner familiar with the technology. After determining what the invention is alleged to be, the examiner conducts a search of the Office records to ascertain whether it is the same as, or obvious in view of, technology already described in earlier domestic or foreign patents or other technical literature (known collectively as the prior art). The examiner also determines whether the invention has utility and whether it is clearly described in a way that teaches others how to make and use it.

The examiner then communicates the initial conclusions on patentability to the applicant. This communication, known as the first Office action, explains the reasons why the examiner considers the claimed invention unpatentable, if that is the case. The communication also contains copies of any relevant prior art found in the search. Additionally, the first action points out any formal deficiencies in the application and, if possible, offers suggestions on how the invention could be more precisely defined. It also identifies any problems with the completeness of the description, the utility of the invention, and may suggest how the claims could be amended to overcome their rejection. A reasonable period is provided for a response from the applicant.

In a small percentage of cases, the first Office action indicates that the invention is patentable and that all formal requirements for the application are met. Accordingly, the application can be processed for the granting of a patent. In the more typical situation, however, some or all of the claims are rejected as unpatentable, the description found deficient, or both. The applicant must respond directly to the objections and rejections of the examiner. The response may include amendments to the claims and arguments as to why the examiner's conclusions are deemed wrong.

If the applicant's response successfully disposes of all of the examiner's concerns over both formal and substantive issues, the application is processed for grant of a patent. On the other hand, the examiner and the applicant may reach an impasse over patentability. If so, the examiner sends a final rejection to

the applicant explaining the Office's stance on the unresoloved issues. This final rejection generally closes the prosecution of the application before the examiner.

An applicant dissatisfied with the final rejection may appeal to the Office's Board of Patent Appeals and Interferences. An appeal is normally heard by three Board members, although an enlarged panel can be convened to hear cases of special importance or difficulty. An oral hearing may be obtained by the applicant, or he may choose to allow the Board to rely on his own brief and the examiner's reply thereto.

If the decision of the Board is still adverse to the applicant, an appeal may be taken to the United States Court of Appeals for the Federal Circuit or a civil action may be filed against the Commissioner in the United States District Court for the District of Columbia. The Court of Appeals may affirm or reverse the Office's decision on the basis of the record. In a civil action, the applicant may present new evidence to the Court for consideration in deciding patentability.

Ultimately, a little fewer than two-thirds of the applications issue as patents. The remaining ones are abandoned by the applicant, usually as a result of an examiner's determination that the subject matter is not patentable. Once a patent is issued its term runs for 17 years. Maintenance fees are due 3 1/2, 7 1/2 and 11 1/2 years after the original grant and must be paid to keep the patent in force.

The volume of applications filed has been steadily increasing over the years. During FY 1987, a record 126,597 patent applica-

tions, excluding designs, were filed -- up almost 5,000 from the previous year's all time high of 121,611. Examiners disposed of 126,189 cases. Patents, issued excluding designs, totaled a record 82,635, up substantially from 71,791 in FY 1986.

Because we are very aware of the need to issue patents as promptly as possible, the Office continued its drive to reduce to 18 months the average time for final action on a patent application. Eighteen months is about the shortest pendency time during which a complete and thorough examination can be conducted, including a fair and reasonable opportunity for the applicant to respond to the conclusions reached by the examiner. However, because of the increased workload, coupled with funding reductions under Graham-Rudman-Hollings in FY 1986, we were forced to extend the target date for achieving the 18-month goal to the end of FY 1989. Still, 5 examining groups have already reached and are now maintaining that goal. Despite the increased workload, average pendency time for utility, plant and reissued patents decreased during FY 1987 to 20.8 months, down from 22 months at the beginning of the year, and now stands at 20.3 months.

Although our efforts have proved successful in the continued reduction of average pendency time for utility patents, applications in the field of biotechnology have not fared as well. As a matter of fact, application backlogs in the biotechnology area continued to increase, despite additions to examiner and supporting staff. Because the reasons for this increase are many, I will highlight only the most important ones. First, patent applications in that field are filed at a rate that has been increasing substantially faster than that in other areas of

technology. Given the relatively small pool of examiners fully experienced in biotechnology, our capacity to absorb and train new examiners in this area was limited. Considering the narrow and specialized nature of the technology, examiners require a long learning curve before they are fully productive and our capability to shift examiners from other areas is limited.

The backlog may also have been exacerbated by the fact that the lion's share of biotechnology examination was conducted by the largest group in the Office where it had to compete for management attention with other large and growing areas of technology such as pharmacology and organic chemistry. This caused conflicting priorities, and ultimately management problems. Lastly, the overall backlog problem in biotechnology was not easily recognized, given the fact that the technology was fragmented over four different examining groups. As a consequence, specific backlogs in the field of biotechnology were masked in the overall backlog, or lack of backlog, statistics of those other groups. Fortunately, we have recognized the problem and are well underway to redress the situation.

When about three years ago we first realized that a backlog problem existed in the biotechnology area, we attempted correction through the hiring of new examiners for this field. This did not, however, alleviate the problem. After reassessing the situation about a year ago, we determined that a more drastic plan of action, including the creation of a new examining group, was necessary. We have been implementing this plan for the past year and Assistant Commissioner Tegtmeyer recently discussed its specific points with staff members of the Subcommittee. The plan

addresses not only the backlog problem, but also the need to maintain a high quality examination.

Our action plan consists of steps that would not only shift and consolidate available examining resources, but also increase those resources for the biotechnology area from within the Office and from the outside. Most important was the decision, as I have mentioned already, to establish a new group that would deal exclusively with the field of biotechnology. In the first instance, this has meant the consolidation of art and examiners from four groups into the new biotechnology group. Our plan also calls for identifying qualified examiners throughout the Office who can be transferred to the new group and be retrained to examine biotechnology applications. Further, a larger proportion of newly hired examiners will be assigned to this new group, than will to any other group in the Office. The hiring level established is the maximum that the group can absorb.

To attract and to retain good talent and to put biotechnology examiners on a par with examiners who are engineers, we want to obtain special pay rates for new examiners in this area. To permit the most efficient application of our examining resources, we have accelerated, intensified and enhanced technical and legal training for these examiners and we are improving their search tools needed for efficient production and quality examination. With these and other points in our plan we are addressing the problem in every way we can.

Recently, we conducted an analysis to determine the turnover of examiners in the art units that until now were mainly concerned

with the examination of biotechnology applications. This analysis shows that, over a five year period, the attrition rates in those units for junior examiners are not any greater than those in other examining units. However, as I have mentioned, we are requesting special pay rates for new examiners in this field. Still, it will always be difficult to compete with the private sector in the biotechnology area, considering the high salaries offered there, especially in the patent field. We are not likely to retain examiners, even with extraordinarily high salaries, as the private sector would most likely match and exceed our salary offers and make available substantial fringe benefits that cannot be matched in government service. Even so, faced with considerable difficulty in recruiting new examiners for the field of biotechnology, we have been successful in attracting quality professionals.

As I have already noted, we are reducing the pendency time of patent applications across the board. The delayed obtaining of patent protection is not just detrimental to the biotechnology industry, it works to the detriment of industry as a whole. Any time that patent pendency is unduly long, protection is delayed, information about competitors' patent rights is delayed and the disclosure of new patent technology is delayed. Over the long run, this may tend to inhibit the development of new technology, or possibly result in wasteful duplication of research and development efforts. We did not consider automatic publication of applications 18 months after their filing or priority date to be a good answer to these concerns. Aside from the increased costs to the public and the Office, automatic publication destroys the confidentiality of the subject matter disclosed in

the application. This denies inventors the option to keep their invention secret if they could not obtain patent protection and especially if they only filed in the United States. Frankly, these considerations convinced us back in 1982 to embark on a pendency reduction program to 18 months for all patent applications.

However, while we were fighting the backlog problem, relief has been available all along for companies who need a patent quickly, particularly those that are thinly capitalized and may depend on patent ownership to attract additional investment capital. Although applications are generally examined in order of their receipt, we have had a longstanding procedure to ensure that this examination process does not work to the detriment of applicants who are in need of speedily obtaining patent protection. Examination can be obtained out of turn in circumstances such as the advanced age of the inventor, ongoing infringement of the invention, reliance on the patent for investment decisions or the nature of the subject matter. In addition, every application that has not yet received an examination is eligible for an accelerated examining procedure if requested and if certain, relatively uncomplicated, procedural requirements are met. Accordingly, no application is necessarily condemned to have to await its regular turn for examination, nor do patent applicants have to bide their time until we win the battle of the backlog.

Given the existence of this program, which has the potential to reduce pendency for time-important applications significantly, we are frankly puzzled over its negligible use by applicants in the biotechnology field. Of the over 5,000 biotechnology

applications filed in 1987, applicants filed petitions for an accelerated examining procedure in only 17 applications.

As part of the program to reduce the overall pendency of patent applications to 18 months, we requested and have received funds since 1982 to hire additional examiners. While our funds have been sufficient over that time period, funding for fiscal year 1986 did fall short due to the spending cuts imposed by Graham-Rudman-Hollings. During that year only 94 examiners were hired and 10 of them were assigned to examine applications relating to biotechnology. This number was considerably below the overall hiring effort that was needed to keep backlogs in various areas of the Office under control.

Despite our overall backlog, and specifically that in biotechnology, all the steps to redress this problem have been taken with an eye toward maintaining, or even enhancing patent quality. In newly emerging technology areas, such as biotechnology, robotics and superconductors, special programs have been implemented to prepare examiners to handle the rapidly growing number of patent applications. The program includes focused training, search file enhancement and other steps, such as improved access to on-line data bases on biotechnology. In addition, we recognized that the complexity of biotechnology demanded more examination time per application to ensure a quality product. As a consequence, examiners in this field have been allotted more time to work on these applications. To enable us to control the quality of issued applications, we instituted a review program years ago under which 4% of all issued applications are scrutinized once more to determine whether the claimed invention is

patentable and whether a patent should issue. In addition, we have recently instituted a quality reenforcement program to see where further improvements can be made in our patent examining procedures.

All these efforts to attack our backlog and to reduce the pendency time of applications do not call for additional budget funds at this time. Our specific plan to reduce pendency in the biotechnology area is relatively small in cost. We would, therefore, not recommend that fee revenues from patent applicants be increased for this purpose, nor do we feel it appropriate or fair to demand higher fees for applications relating to a particular technology.

Because of the high rate of filing of biotechnology applications, we will not be able to reduce their pendency to the 18-month period by the time expected for the rest of the Office. However, by putting our present plan of improvement into effect, we can expect the new biotechnology group to reach an average pendency time of 18 months by FY 1993 or 1994, if we can assume that the filing of biotechnology applications will continue to increase at the current rate in the range of 12-15% for the next few years, and then begin to taper off in the early 1990s to a range of 9-11%. At this time, we feel this is a realistic projection, as are some of the other assumptions inherent in our present plan. Naturally, should these assumptions and projections change, our plan would have to be modified to successfully continue our attack on the backlog of biotechnology applications.

Our plan, however, should not include options such as the splitting of filing and examination fees or the use of internal

priority documents. Both of these options might result in increased filings and in the end produce the same or even higher examiner workloads. Splitting the filing and examination fees, coupled with an extended period to request examination, would amount to a deferred examination system. This would not enhance our goal of early dissemination of information to the public, early information about competitors' patent rights and early patent protection. Even automatic publication of the application at 18 months would not resolve all of these concerns, but would result in higher costs to the public and the Office.

The use of internal priority documents would, in our opinion, also tend to worsen the backlog situation in biotechnology. Such a program would tend to stimulate increased initial filings with the potential of perfecting those applications at a later time. This is not to say, however, that we are rejecting suggestions of this nature out of hand. At this time, we are investigating the patent processing systems used in Europe and Japan which may offer certain other advantages to patent applicants. We are also exploring these possibilities as part of an effort to harmonize our patent system with those of other countries. These efforts are coordinated by the World Intellectual Property Organization in Geneva, Switzerland, and are also conducted on a trilateral basis between our Office and the European and Japanese Patent Offices. In this respect, we continue to try to serve the public by providing quality patent protection and a reasonable period of application pendency.

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Testimony
U.S. Patent Office Backlog and the Biotechnology Industry

Linda I. Miller
First Vice President
PaineWebber Incorporated

100th Congress
United States House of Representatives
Committee on Small Business
Subcommitte on Regulation and
Business Opportunities

March 29, 1987

Mister Chairman, distinguished members of this committee and staff, I would like to thank you for the opportunity to address the important issue of the U.S. patent office backlog and its effect on the prospects for the growth of our domestic biotechnology industry. The House Committee on Small Business is providing a valuable forum in which to examine this pivotal issue, one on which the ultimate success of the emerging biotechnology may depend. The protection of property rights is of critical concern for the small businesses comprising the the biotechnology industry. These firms and the scientists and entrepeneurs they employ are investing in high risk product development programs which are beginning to exert important beneficial influences on our society. The security of a return on these investments, both financial and human, should be guaranteed through our patent system as have returns to other industries been protected through the history of our nation.

I will first introduce myself and as a representative voice for the financial community I would like to provide an overview of the prospects for this important and youthful sector of our economy. I would like to stress the three major concerns that the financial community has with regard to the patent backlog in biotechnology: its encouragement of unfair competition between firms large and small, its influence on corporate misallocation of resources, and its effects on technology transfer from our domestic industry and from our small businesses to foreign corporations and large multinational drug and chemical companies. I will then review some of the pertinent financial facts regarding the biotechnology industry, highlighting the magnitude of investments in research and development made by this emerging industry as well as the level of job creation it has offered. Then, I will address the financial community's perception of risks for this industry which you will see is inextricably linked to patent concerns. Finally, I have selected several examples illustrating the financial community's reactions to patent uncertainties in biotechnology.

Introduction

To introduce myself, I am Linda I. Miller, First Vice President of PaineWebber, a brokerage and investment banking firm headquartered in New York. I have followed the biotechnology sector as an investment research analyst since 1980, when Genentech, a leader in this field, became a publically held company. I have had the opportunity to follow from a close observation perch, the ups and downs of this promising sector. As further introduction, with nearly 300 offices across the United States, PaineWebber provides investment services for more than one million persons in this country. Since 1980, when PaineWebber managed the initial public offering for Genentech, we have raised approximately $800 million for companies in the biotechnology field. And PaineWebber currently supports OTC marketing making activities in nearly 3 dozen biotechnology stocks. From this commitment you may gather that PaineWebber believes strongly in the future of the biotechnology industry. With the enormous power and elegance of these new scientific techniques many of which were developed through our unexcelled public funding programs for basic research, the creation of quality entrepeneurial groups devoted to product commercialization, and backing from the U.S. financial markets which have been willing to fund these high risk ventures, biotechnology represents an important opportunity for the United States to remain competitive within the global economy.

Future of the biotechnology industry

The future of the biotechnology industry remains extremely promising. The ability of new techniques, including monoclonal antibodies and recombinant DNA to generate novel and useful new products has been established. Nearly two hundred products have been approved by the FDA for marketing from this field. Many are well known such as tissue plasminogen activator, alpha interferon, hepatitis B vaccine and human growth hormone. Other, less well recognized products have provided us with improved therapies for organ transplant patients and faster, more sensitive at home pregnancy tests. Sales of these products which totaled $400 million to $450 million in 1986, rose to $650 million to $700 million in 1987 and may exceed $1 billion in 1988. With 80 public companies competing in this marketplace, a significant number of opportunities are yet to be commercialized.

Concerns with the U.S. patent backlog

The financial community clearly questions the support offered to the biotechnology industry from the U.S. patent system -- including the U.S. Patent and Trademark office. We are disturbed by the backlog in reviewing and granting biotechnology related patents in the U.S. The escalating number of total applications pending, now approaching 7,000 and growing at a rate in excess of 20% annually is undermining the viability of this industry.

Encouraging unfair competition: Many important products have been developed and some are even sold in the market today without the benefits of patent protection. Genentech's Activase, tissue plasminogen activator, is a prime example of entepreneurial determination and commercial success not matched by property protection offered by our patent system. With more than 20 competitors in the race to develop t-PA based thrombolytic agents, small company "Davids" are pitted against many me-too "Goliaths" without benefit of the "slingshot" of patent protection. How many companies such as Genentech can afford to invest $200 million in a competitive product development program without the known benefits of patent protection?

Inefficient allocation of resources: With the lack of clarity of property rights in biotechnology in the United States, many companies are developing similar products—expending valuable resources, both human and financial—on me-too programs. In 1985 there were more than two dozen companies developing alpha interferons in the U.S. When patents were issued and commercialization rights granted in the U.S., we estimate that more than half of those programs were terminated. Now two companies in the marketplace, Hoffmann-La Roche which licensed its product from Genentech, and Schering-Plough which licensed its product from Biogen, have cross-licensed patents and benefit from those technical developments. We will never know if small companies like Biogen and Genentech would have maintained product development rights with an earlier clarification of the alpha interferon patents. Nevertheless, with a swifter resolution of the patent positions in this field, many companies and scientists might have devoted valuable resources in other more profitable directions.

Reliance on funding through technology transfer from the U.S.: Investors are forced to make decisions without understanding property rights in biotechnology. As a result, the returns that we demand from our investment are inordinately high, the volatility to which stocks are subject is extreme, and the public' participation in the rewards of this industry are limited. On the other hand, funding needs of the domestic biotechnology industry continue to escalate. Often the sources turned to when the U.S. equity markets are unapproachable are major U.S. or even foreign corporations. These partners often extract technology transfer rights in addition to a high return on investment. The original research giving birth to these product development programs may have been funded by the U.S. government at academic research institutions. Many small biotechnology companies have been forced to rely heavily on foreign partners. In 1986 between 15% and 20% of the revenues of our U.S. biotechnology industry were derived from foreign partners. For some companies the amounts were as high as 50%.

Financial overview of the biotechnology industry

I would like to review some of the pertinent financial facts regarding the biotechnology industry highlighting the magnitude of investments in research and development made by this industry as well as the level of job creation offered.

During the period 1984 through 1986, a composite of three dozen publically held biotechnology companies spent nearly $850 million on research and development. This understates the total amount spent on research and development in biotechnology by omitting several small companies as well as all private companies for which data is not available and large drug and chemical companies which include biotechnology as only a portion of their entire research budget. These funds were expended on urgent problems facing society: medical research in new cardiovascular agents like t-PA, anticancer drugs like interferons and AIDS products, importantly diagnostic tests to preserve our blood supply and growing programs in AIDS vaccine and therapeutic developments. We anticipate that in 1987, for which full financial figures have not been reported, the industry will expend approximately $400 million to $450 million on research and development. Of course, this figure does not match the expenditures made by major drug companies in the U.S. which totalled $3.1 billion in 1986. Nevertheless, this industry is expending funds on research at 120% of its rate of revenue generation--while the major drug companies spent 9% of revenues on research and development in 1986.

Job creation has been significant in biotechnology. We estimate that nearly 8,000 jobs have been created in the biotechnology industry through the end of 1986. Again, this figure is understated, but we expect it to increase to between 9,000 and 10,000 through the end of 1987. Of course compared to the number of employees in the pharmaceutical industry of 335,000 this is a minor amount. But the drug industry totals have been shrinking an average of 1% per year during the past five years, and of course include a significant number of non-U.S. employees. As biotechnology-related products are introduced, we expect this figure to increase at a faster rate. For example, Genentech, the most mature company in the biotechnology industry, had supported employment growth from 670 employees in 1984, to 890 employees in 1985, to 1,170 employees in 1986 and an estimated 1,650 employees today--a growth rate of 35% annually.

Patents: a major risk for the biotechnology industry

We reviewed the investment "risk factors" cited for the companies in the industry in nearly four dozen public offering documents filed with the Securities and Exchange Commission in 1986 and 1987. As you know, in offerings of speculative investments a section highlighted as risk factors is included in prospectuses. We analyzed the risk factors cited - which totaled more than forty - from regulation to lack of dividends to seasonal sales patterns. The ten factors listed most frequently and highlighted in Table 1 are: competition, patents/proprietary technology, government regulation, attraction/retention of key personnel, technological change, early stage of product development, possible stock volatility, history of financial losses, future capital requirements and product liability.

The survey reveals that risks for the industry are heavily linked to patent concerns. Among all factors surveyed, patents and proprietary technology was listed as a risk factor most frequently—except for competition. Patent risks were mentioned in 93% of all offering documents as a factor that the investor should consider while competition was mentioned n 95% of all cases. Other critical issues cited were government regulation and attraction/retention of key personnel. When we weighted the risk factors for the order in which they were mentioned in the prospectuses—an indication of severity of the risk—patents were viewed as more important than government regulation, attraction/retention of key personnel, stock volatility and product liability.

Illustrations

Finally, I have selected several examples illustrating the financial community's reactions to patent uncertainties in biotechnology. It is difficult to demonstate that the absence of patent protection has a profound influence on stocks—there are no events to chart. However, I have charted several major patent related announcements which have occured during the past three-to-four years, and show that the markets respond significantly to patent announcments.

In Exhibit 1, a recent case, we see the effects on Genentech's stock from the U.S. Patent Office granting a patent referred to here as "Riggs Itakura" which represents a broad, enabling technology in the field of recombinant DNA. It was awarded to Genentech in early November of 1987 and as you can see, the stock smartly outperformed the market after the patent was granted.

A second example in Exhibit 2, is Cytogen Corporation, a company developing monoclonal-antibody based products for medical imaging and cancer treatment. The company developed a novel system for linking their antibodies to active ingredients—anticancer drugs, imaging isotopes or other agents. When a patent was granted in early June of 1987, the stock moved up outperforming the overall stock averages.

In the third Exhibit, Cetus Corporation, a company developing interleukin-2, a product with potential as a anti-cancer agent is also shown outperforming the market. In February of 1985 the company announced that it received a patent for its product, a modified form of interleukin-2. You can observe from Chart 3 that Cetus' stock jumped on that announcement and significantly outperformed the Standard & Poor's 400 index during that brief period.

Another example is Exhibit 4, highlighting the dates when Hoffmann-La Roche, a licensee of Genentech and Schering Plough, a licensee of Biogen crosslicensed patents that each held related to alpha interferon. Clearly the stocks of both license partners, Genentech and Biogen outperformed the market after the announcement. We attribute this to the degree of property rights protection perceived in the market from the patents and respect for patents indicated by these companies.

Another Exhibit, number 5, indicates the reaction of two stocks to a reversal in the United Kingdom courts of an issued patent for Genentech's t-PA. The patent was challenged by Burroughs Wellcome, a licensee of Genentics Institute. We observe that not only did Genentech's stock suffer after the reversal of the suit, and Genetics Institute's stock outperform the market, but both stocks subsequently lagged an overall upward trending market. This highlights the fact that patent uncertainty--be it from overturned patents or unissued patents--is of greatest concern to the financial markets.

Our final Exhibit 6, shows as well that patent uncertainty, in this case brought on by litigation, can cause stock values to decline. The case in this instance in Cetus and Amgen, both developing versions of interleukin-2, an anti-cancer product. Two lawsuits filed in Agust and September of 1986 coincided with depressed values of both stocks.

Thank you for this opportunity to comment on the patent backlog from the vantage point of the financial community. I am hopeful that the diligent efforts of this committee will build a stronger patent system for the domestic biotechnology industry. The U.S. investor will benefit as well from the preservation of another competitive industry in our economy.

Table 1 Biotechnology company "risk factors"

Factor 1	Frequency of inclusion in SEC filings
Competition	95%
Patents/proprietary technology	93
Government regulation	89
Attraction/retention of key personnel	82
Technological change	77
Early Stage of product development	73
Possible stock volatility	66
History of financial losses	64
Future capital requirements	55
Product liability	55

Exhibit 1

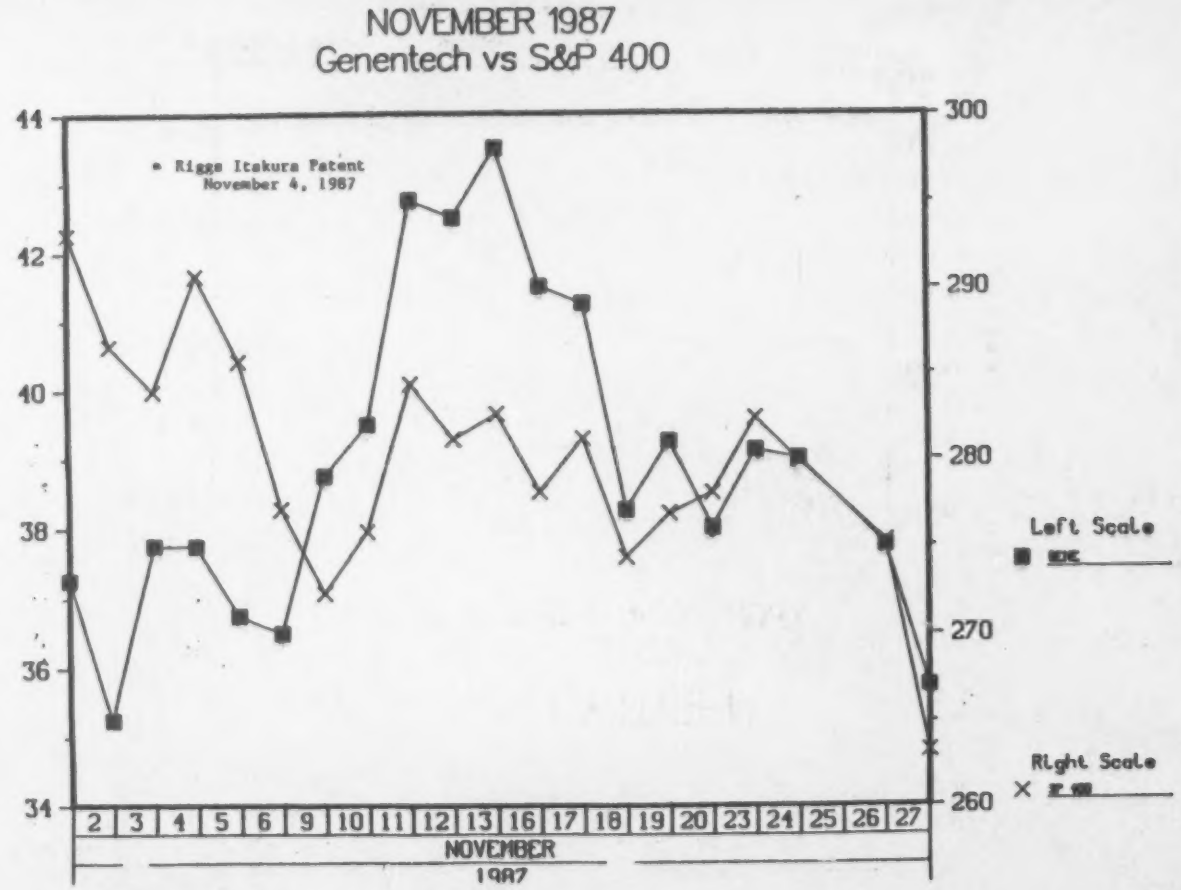
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Exhibit 2

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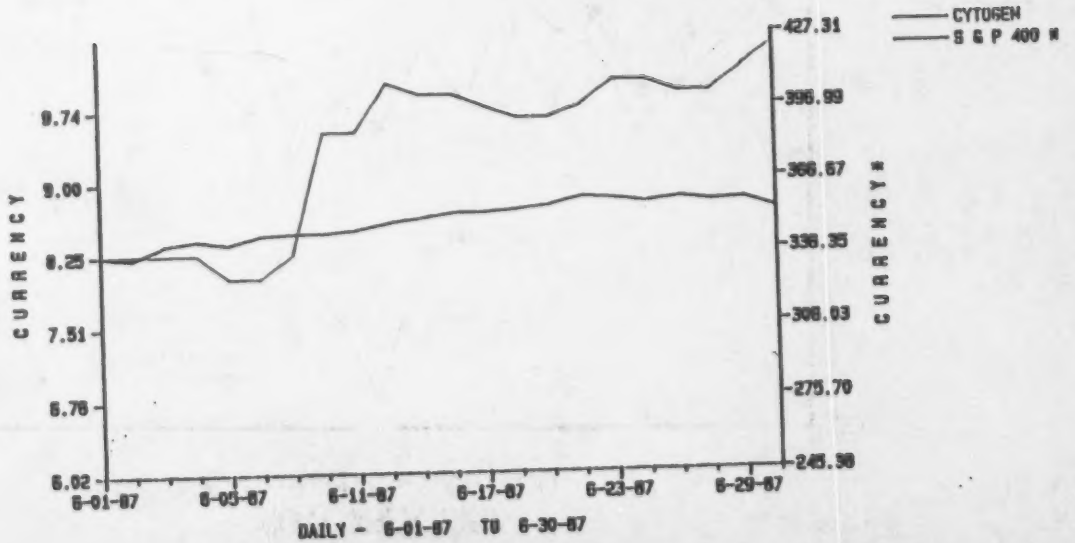

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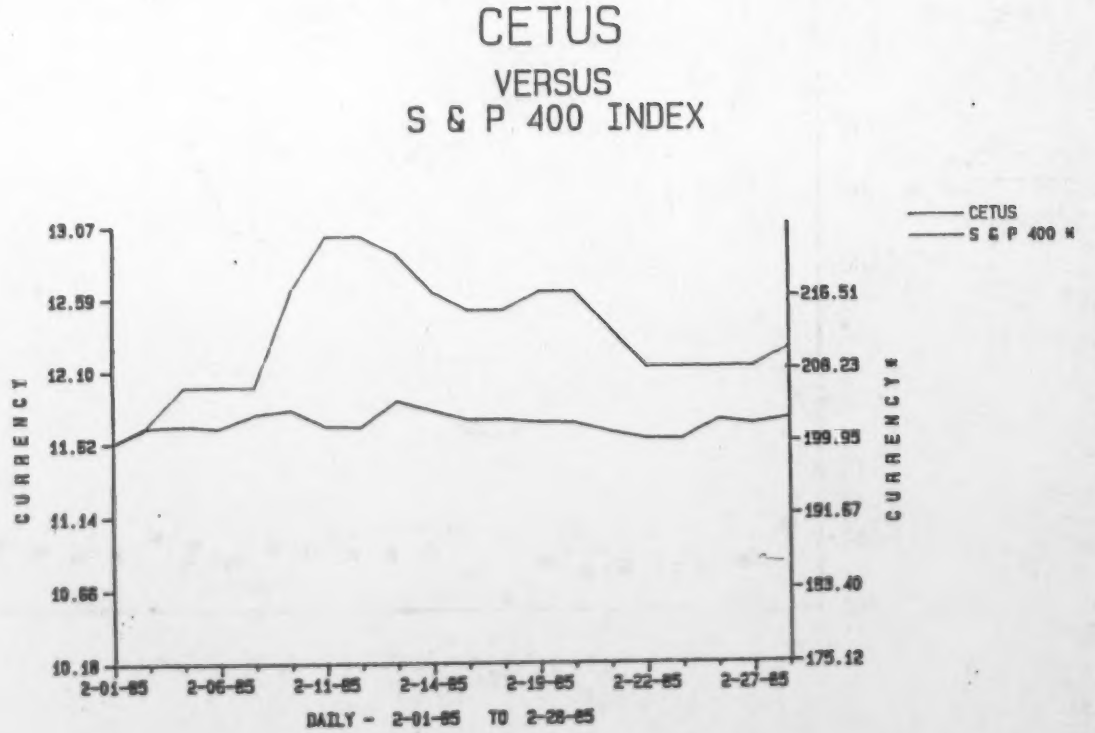
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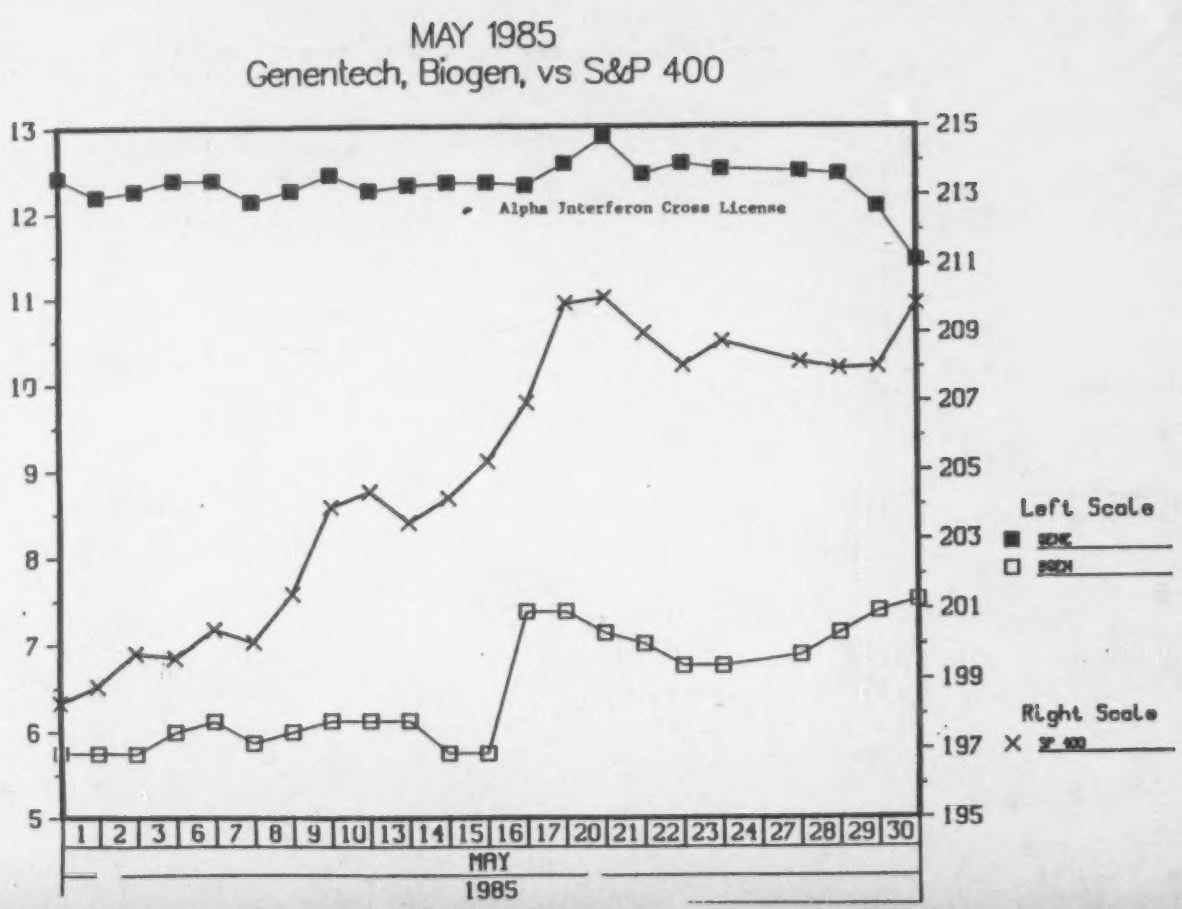
Exhibit 4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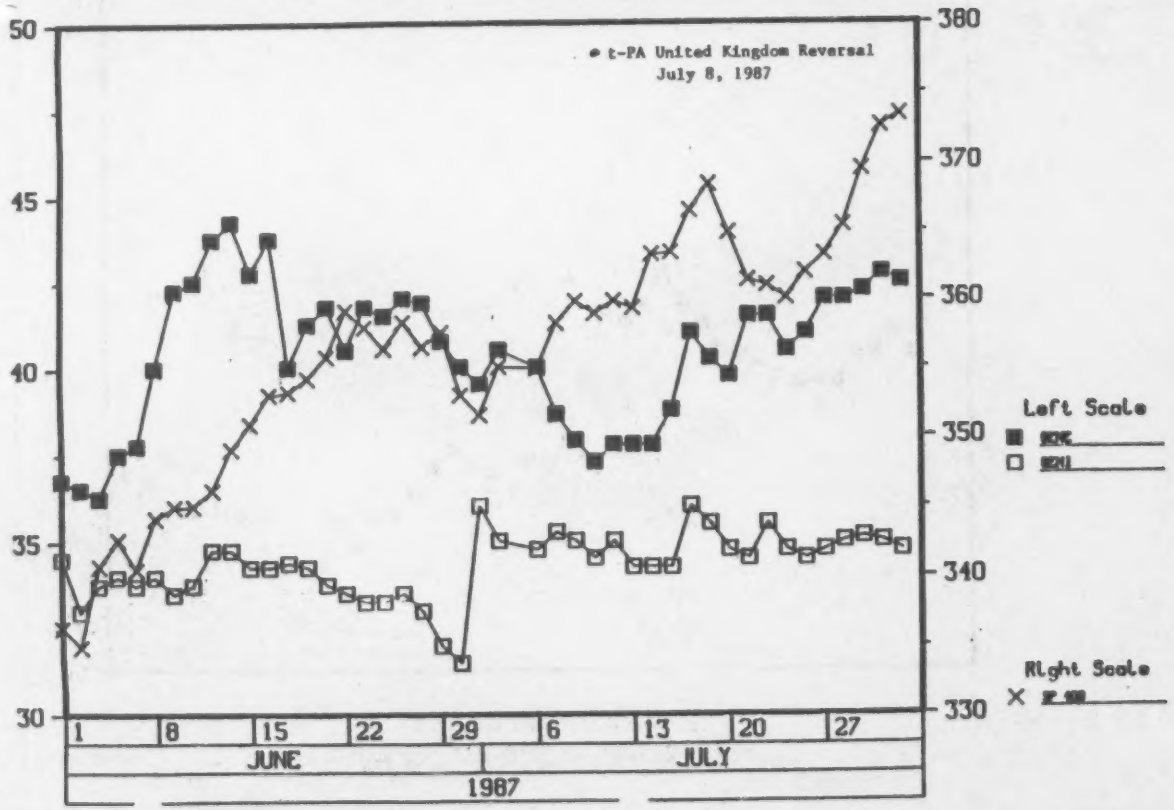
X S&P 400


JUNE - JULY 1987
Genetics Institute, Genentech vs S&P 400
t-PA United Kingdom Reversal
July 8, 1987
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JUNE
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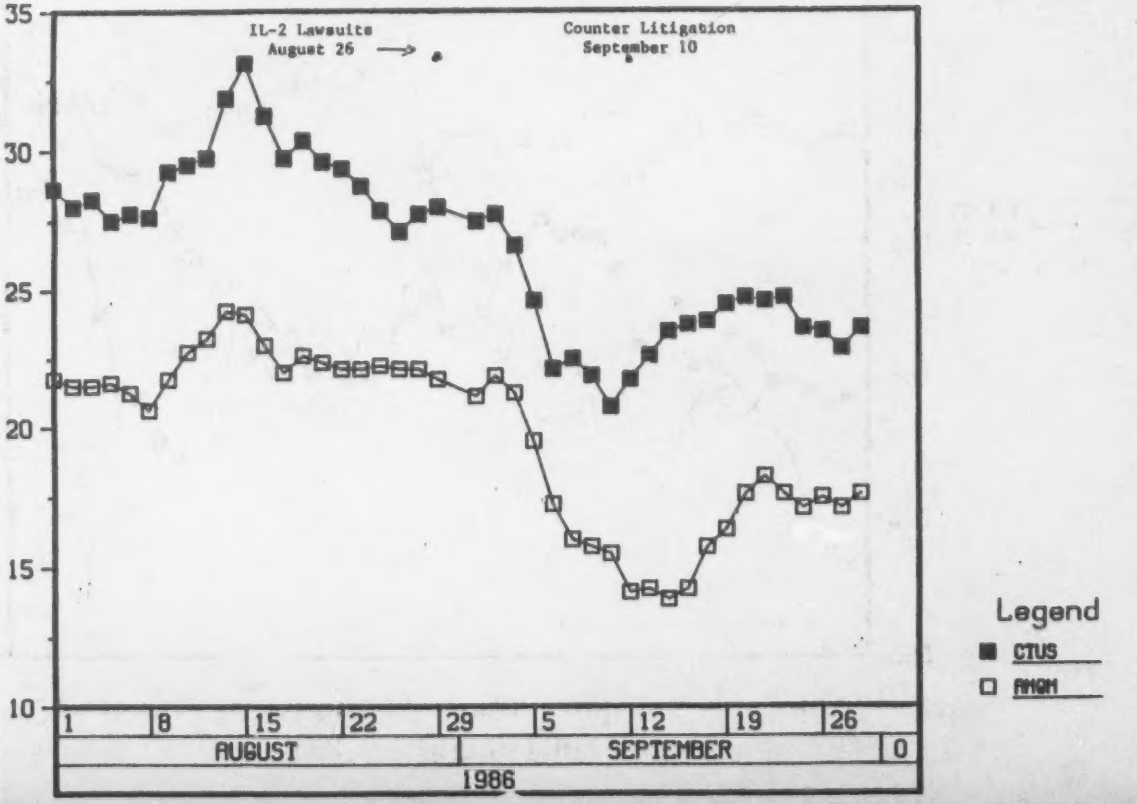
1987

Exhibit 6

AUGUST – SEPTEMBER 1986
Cetus vs Amgen



STATEMENT OF GEORGE B. RATHMANN

PRESIDENT AND CHIEF EXECUTIVE OFFICER

AMGEN, INC.

BEFORE THE

SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

OF THE

HOUSE COMMITTEE ON SMALL BUSINESS

HEARING ON

THE BACKLOG IN BIOTECHNOLOGY-RELATED

PATENT APPLICATIONS

TUESDAY, MARCH 29, 1988

George B. Rathmann is currently the President, Chief Executive Officer and Chairman of the Board of Amgen, Inc. Before joining Amgen, Dr. Rathmann was Vice President, Research and Development, Diagnostics Division, of Abbott Laboratories, which he had joined in 1975. Previous experience included Litton Industries, as President of Litton Medical Systems, Inc., and with the 3M Company where he served in various scientific and management positions over a period of 20 years. He received his B.S. in Physical Chemistry from Northwestern University in 1948 and his Ph.D. from Princeton University in Physical Chemistry in 1952. He is a member of the American Association for the Advancement of Science, American Chemical Society and since 1982 he has served as an Officer and Board member of the Industrial Biotechnology Association and currently serves as Chairman.

Summary of Presentation

It is my understanding that the Constitution instituted the U.S. Patent system on the belief that the public will benefit by encouraging invention and its disclosure and that rewarding the innovative forces in society can best be accomplished by granting limited exclusive rights to inventions. Biotechnology has been a major force for the creation of new products to the benefit of society. The United States is in a leadership position in the discovery and development of these products largely as the result of the formation of small independent biotechnology companies that have pioneered most of these innovations.

My prepared testimony addresses the factors that led to these developments and the role of patents in stimulating the financing of the research and development being conducted in these companies. I have outlined the typical history of such a company, and the critical importance for the viability of such companies that the making, using and selling of the products of such research be provided with appropriate patent protection. Increasing backlogs in the processing of patent applications will have serious deleterious effects on continuing investment and the maintenance of the United States' leadership position in biotechnology.

It is strongly recommended that immediate additional resources be allocated to the patent office to meet the needs of acquiring adequate, highly trained examiners to reduce the backlog and expedite appropriate patent protection. Biotechnology has already provided thousands of patients with the benefit of unique products that were unavailable prior to the discoveries of this industry. The future holds even greater opportunities for all of the peoples of the world if additional inventions and discoveries can be encouraged by the timely issuance of patents protecting this intellectual property.

Good morning Mr. Chairman, members of the Subcommittee and fellow panel members. Let me say at the outset that I appreciate the opportunity to set forth my views on the current backlog in biotechnology-related applications in the patent office.

Introduction

I am George Rathmann, the President and Chief Executive Officer of Amgen, a biotechnology company in Thousand Oaks, California. My testimony will cover a brief history of our company which is typical of many of the 200 biotechnology companies formed in the early 1980's. I will give special attention to the role of patents in the raising of capital and the potential generation of profits to provide a satisfactory return on the significant investments often made years before any tangible products can be discovered and sold.

A major thrust in biotechnology is the development of products based on the techniques of recombinant DNA, frequently referred to as genetic engineering. In discussing patent issues, I will deal primarily with that field which has presented particular challenges to all patent offices around the world. I will then be happy to discuss potential improvements that could ensure appropriate protection for the innovations that have been pioneered by U.S. companies and will bring important benefits throughout the world.

I joined Amgen as the first employee late in 1980, the year of our founding. You will recall that that was the year that the Supreme Court ruled that living organisms could be patented, and shortly thereafter, Genentech raised roughly $35 million in its initial public stock offering. My first job was to raise money to fund research and development at Amgen. We completed an initial private stock placement, raising $19 million in February of 1981. Our investors expected that it would be at least five years before we had products on the market but that these products warrant patent protection and would promise the types of benefits to society that would justify sufficient profit margins to bring a return on their investment made many years before. Our research and development costs for the first two years resulted in large losses which consumed virtually all of the $19 million. The money had been spent to attract top talent in molecular biology and other leading edge biological sciences. The commitment of these young scientists created a dynamic environment and produced a significant number of patentable discoveries during this first two years.

Amgen was not alone. By 1983, more than 100 biotechnology companies had been formed. These small companies were clearly in the lead in the discovery and announcement of new molecules derived from genetic engineering. The extraordinary value to humankind of these discoveries stimulated a new round of investment in 1983. Investor confidence in Amgen and other companies permitted each of us to achieve several more years of

financial stability and paved the way for the major discoveries in the mid-1980's.

By 1985, over two dozen new materials were entering human clinical trials for cancer therapy, antiviral therapy, treatment for blood cell deficiencies, anti-hypertensives and vaccines. Four products were already on the market. Small U.S. independent biotechnology companies played the lead role in virtually every single one of these discoveries. Initial patient responses were dramatic including the first clear cure for the deadly cancer, hairy cell leukemia, correction of anemia with a response rate greater than 95% and little or no side effects and many others. The leading companies were expanding rapidly and these dramatic results paved the way for major investments. Since its inception, Amgen has raised $300 million and we will not market our first pharmaceutical product until later this year.

What has been the impact of patents? The anticipation of patent protection for the revolutionary pharmaceutical products produced by recombinant technologies has provided the investment incentive that has financed biotechnology companies. Licensing patents, even at the application stage, provided a means of bringing in needed cash years before the product would be on the market. The publication of these patent applications overseas within approximately twenty months from the time of U.S. filing represents the largest single body of detailed technical instructions for the preparation of new, important genetically

engineered materials. This information, representing billions of dollars of U.S. investment and innovation can thus be freely examined by anyone in the world. The patent systems around the world are designed to provide the scientists and their selected assignees seventeen years of exclusive use of these inventions in exchange for this information. This should mean protection for the materials, the processes, and the useful products embodied in these patent applications. Much as the Supreme Court wrestled with the issue of the patentability of a living organism, so have the world's patent offices deliberated over how to apply the patent system to the products of biotechnology. In many countries including the United States, these protracted deliberations are placing in jeopardy the rights of these pioneering inventors.

The teachings of such a patent application is sufficient to provide for rapid and obvious minor molecular modifications which must fall within the scope of the claims of the patent or there will be no useful protection for the inventor. Patent examiners highly trained in molecular biology will be necessary for accurate and proper determination of patentability. Such scientifically trained individuals are in demand around the world and patent offices face increasing backlogs as a result. Our experience has been that patent examiners in the U.S. are experienced, conscientious, and overworked. Occasional turnover has resulted in months of disruption of communication and significant delays in the prosecution of our cases. The

precedent setting nature of some of the patents may also lead to significant delays.

Would rapid appropriate patent protection for U.S. inventions within the U.S. adequately protect the U.S. leadership in biotechnology? For worldwide protection, it will naturally be necessary for patent offices around the world to follow the U.S. leadership. In any event, U.S. protection would at least prevent importation of products from other countries that will seriously affect the economic viability of U.S. biotechnology companies.

Considering the billions of dollars invested in biotechnology (the current market value of biotechnology companies is in excess of $8 billion), I support the addition of resources to the U.S. Patent Office promptly and effectively and at levels in keeping with the tremendous stake the U.S. has in the protection of its intellectual property.

I will be pleased to answer any questions. Thank you for the opportunity to speak with you today.

GRL:letSJ

STATEMENT OF ROBERT P. MERGES

JULIUS SILVER FELLOW IN LAW, SCIENCE & TECHNOLOGY

COLUMBIA LAW SCHOOL

BEFORE THE

SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

OF THE

HOUSE COMMITTEE ON SMALL BUSINESS

HEARINGS ON

THE BACKLOG IN BIOTECHNOLOGY-RELATED

PATENT APPLICATIONS

Tuesday, March 29, 1988

Robert P. Merges is currently the Julius Silver Fellow in Law, Science & Technology at Columbia Law School. He received his LL.M. degree from Columbia after practicing with a law firm in Palo Alto, California that serves primarily technology-oriented companies. He graduated from Yale Law School with a J.D. in 1985, and received a B.S. from Carnegie-Mellon University in 1981. He is an assistant instructor in a seminar on the legal problems of the biotechnology industry at Columbia Law School, a seminar he helped to design. He has written a number of scholarly articles on patent law, and has also published shorter pieces on biotechnology patents for Genetic Engineering News.

Summary

While the present backlog in pending patent applications across all technologies is far from ideal, one important technological sector has an exceptionally large backlog: biotechnology. The current average pendency is longer than four years, and several key patents on basic biotechnological techniques were in the office for longer than eight years.

For many industries, the backlog is a headache; but for a large number of biotechnology firms, it is a major catastrophe. This is especially true of smaller firms that depend on external funding or marketing agreements to commercialize their technology. Without the relative certainty of a patent, creditors, investors (e.g., venture capital firms), and licensees are exposed to a great deal of uncertainty. When this uncertainty is added to the technical uncertainty of most new biotechnology products, sound business practice may dictate that the project not be pursued. In this way, the backlog directly threatens at least the small-firm sector of a most promising young industry.

The solution to the problem must be pursued on several fronts. Congress should increase Patent Office appropriations enough to allow the Office to hire even more examiners than the Office's current plan calls for (i.e., more than twenty-five). Formal on-site training should be formalized and increased, for both new and old examiners alike. Senior examiners should be encouraged to train the new examiners as quickly as possible -- by making each hour of training time count as a fraction of an application disposal, for instance. Several procedural rules should be revised to reduce the "bottleneck" effect, including the rule concerning petitions to make applications "special." Finally, several more substantial changes in patent procedure should be carefully considered: (1) the addition of a two-tier application system, under which an applicant has the option of delaying examination up to 30 months after filing; and (2) extension of the date when a completed application is required after the filing of an initial priority application, from two months to one year.

Good morning Mr. Chairman, members of the Subcommittee, and fellow panel members. Let me say at the outset that I appreciate the opportunity to set forth my views on the current backlog in biotechnology-related applications in the Patent Office.

Introduction

I want to begin by stressing the gravity of the backlog problem to the small biotechnology firm, and to the biotechnology industry in general. First, it must be recognized that a backlog in the Office causes delay in the consideration of new applications, and hence in the granting of patents. For many firms, a delay in the granting of a patent causes problems. This is primarily a function of the uncertainty engendered by the delay; it is difficult for a company to determine whether a product can be sold safely without knowing whether it will be protected against infringement. And even earlier, at the development stage, several firms may be pursuing the same line of research, leaving all of them in doubt as to who has priority of invention. (Interferences and infringement litigation commences only upon issuance of patents.)

So the general picture vis-a-vis backlogs is a bad one. But for firms in a fast-moving technological field like biotechnology, it is even worse. This is because many firms

can be expected to enter such a dynamic field, given the profit opportunities that come with market-expanding innovation. And of equal importance is the rapid obsolescence rate in such fields.

Although the formal patent term may be seventeen years, the true useful life may be considerably shorter. When this is the case, a delay in the granting of a patent can shorten its effective term. This has the effect of diminishing the inventor's reward -- a bad result, given that rewarding inventors (and hence giving incentives to future inventors) is one of the chief goals of the patent system.

For small firms, such as those in the biotechnology industry, the problems of a long pendency period are even worse. This is because these firms depend on transactions with other, usually larger, firms to commercialize their inventions. And patents are a very important element in these transactions.

Investors who may be interested in the technology -- often venture capital firms -- need some kind of asset to justify their investment. Patents, along with trade secrets and, perhaps, the personal services of the startup company's founders, may be all the investor's have to rely on. Even startup companies whose stock is publicly traded rely heavily on patents; before they have any products on the market, investors have little else to go on but announced discoveries, issued patents, and possibly regulatory actions

such as FDA approval for clinical trials. In this context, patents are vital to the financial prospects of these small companies -- even lenders and potential joint venturers keep an eye on these partially patent-dependent stock prices as one indicator of a startup's financial health. (Indeed, stock market prices react very clearly to news concerning a firm's patent position, including applications (when announced), issued patents, and infringement actions.)

In addition, many smaller firms must license their technology to commercialize it. This is because they normally do not have the same marketing infrastructure as larger firms, and cannot raise the money to start one in time to commercialize their product. Patents play a vital role in licensing, usually comprising the primary asset that is licensed. While patent applications can be licensed (as can trade secrets and even know-how), the licensee has less security against rivals in such cases. One of the rivals could have priority, or the application could be rejected for any of the statutory reasons -- obviousness, time-bar, lack of novelty, inadequate disclosure, etc. These uncertainties make the patent application a less-marketable asset than a granted patent. Small companies may thus be denied the opportunity to market their products because of delay in obtaining patents.

Background of the Backlog Problem

The patent backlog problem is by no means a new one. As far back as 1848 Congress expressed dismay at the growing backlog; the Committee on Patents was asked to look into the problem. The Committee report noted that the number of applications per examiner was increasing year by year, and ordered that more examiners be hired.[1] In 1916, the office granted U.S. Patent 1,203,190, which had been applied for in 1880 -- a record pendency period of thirty-six years and nine months. Delays of more than twenty years were also reported in the 1950s.[2]

Thus today's backlog problem in biotechnology must be seen partly as a structural problem, reflecting long-term features of the Patent Office and its staff. Nevertheless, there are reasons to believe the problem has gotten worse since the 1960s. For example, the average tenure of a patent examiner was between five and six years in the 1960s; today that figure has dropped, perhaps to from two to three years. (And it is much worse in Examining Group 120, soon to be Group 180 -- the group that handles biotechnology, where 17 examiners have left in the last two years.)[3] As another example, consider U.S. Patent 4,704,362, issued on November

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[1] See S. JONES, THE PATENT OFFICE 140 (1970).

[2] Id., at 39.

[3] M. Crawford, Patent Claim Buildup Haunts Biotechnology, 239 SCIENCE 723 (Feb. 12, 1988).

3, 1987 to Genentech. This is thought to be a broad, basic patent covering the use of a recombinant cloning vehicle for microbial polypeptide expression. Thor original application was filed in November of 1977, and the continuation-in-part application for the final granted patent was filed in November of 1979. In biotechnology, these eight years were a long and crucial period of development.

Moreover, there is no reason to allow the backlog problem to continue simply because it has persisted throughout history -- especially in the vital area of biotechnology.

Finding Solutions

The solution to the problem must be pursued on several fronts. The most important areas are salaries and training.

Congress should increase Patent Office appropriations enough to allow the Office to hire even more examiners than the Office's current plan calls for (i.e., more than twenty-five). The current plan is designed to get the pendency period down to acceptable length by the mid-1990s. This is simply too long a time frame; many firms could be out of luck between now and then. Indeed, the basic structure of the industry may well have begun to change by that time -- partly perhaps as a result of the backlog -- so that only a few

large firms are left. There is too much of importance for companies today to delay the solution of the problem so long.

Second, formal on-site training should be formalized and increased, for both new and old examiners alike. Senior examiners should be encouraged to train the new examiners as quickly as possible -- by making each hour of training time count as a fraction of an application disposal, for instance. This would allow the senior staff to put their experience to work for the junior staff in the most needed area; it would also help avoid the costly duplication of ad hoc "over-the-shoulder" training of juniors by seniors.

In addition, the possibility of offering a coherent set of courses, rather than an ad hoc grouping, should be considered. Especially if this is designed as an in-house (and after-hours) Master's Degree program, it could serve as a non-salary benefit that would attract new examiners. This should be considered especially carefully if increased salaries are not feasible under budgetary or "equity" constraints.

Several procedural rules should be revised to reduce the "bottleneck" effect, including the rule concerning petitions to make applications "special." These are currently not well-used by patent attorneys, who complain that there are burdensome requirements for gaining a specialness petition. The Office -- or perhaps a committee of the AIPLA or ABA Section on Patents, TRademarks and

Copyrights -- should look into the problem and propose solutions. This would help those firms with large transactions depending on their patents -- e.g., licenses and venture capital funding as menticned above.

Finally, several more substantial changes in patent procedure should be carefully considered: (1) the addition of a two-tier application system, under which an applicant has the option of delaying examination up to 30 months after filing; and (2) extension of the date when a completed application is required after the filing of an initial priority application, from two months to one year.

The first proposal has been described in detail elsewhere.[4] As to the second, it would further the policy of the 1982 patent law amendments. These amendments made it possible for an applicant to submit a "rough application" -- disclosure, claim(s), and perhaps a diagram -- and send in the filing fee and inventor's oath later. The Office has required that the inventor supply the additional matter within two months of filing; the proposal is to lengthen the period to one year. This would encourage the same early filing, but would also give the applicant a post-filing year to assess the merits and uses of the invention himself, before formally prosecuting the patent. The result would be fewer "active" patent applications pending at a given time.

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[4] Wegner, Patent Law Simplification and the Geneva Patent Convention, 14 AM. INTELL. PROP. L. ASSOC. Q.J. 154, 198 et seq. (1986).

Testimony of

HAROLD C. WEGNER
Washington, D.C.

concerning

BIOTECHNOLOGY PATENT APPLICATION PROCESSING

before the

SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES
UNITED STATES HOUSE OF REPRESENTATIVES
COMMITTEE ON SMALL BUSINESS

Rayburn House Office Building
March 29, 1988

Chairman Wyden, and members of this Committee, my name is Harold C. Wegner, Adjunct Professor of Law at Georgetown University. I am also a shareholder in the intellectual property firm of Wegner & Bretschneider.

This Committee is to be congratulated on its continuing interest in the biotechnology problems faced by small American companies.

My testimony today is on my own behalf, neither for any client nor professional association.

OVERVIEW - QUALITY VERSUS "EIGHTEEN MONTHS"

Biotechnology "backlog" problems are self-evident and are interrelated with other serious and already identified problems: Quality control. Personnel turnover. Superficial Examiner actions. Lack of a professional atmosphere. Delayed searches. Delayed patents.

The Chairman and this Committee are to be congratulated on their continuing efforts to aid American biotechnology, particularly the emerging biotechnology companies. The goal of finding solutions, to work with the United States Patent and Trademark Office (PTO), is highly commendable. We have witnessed the problems on a first hand basis; the testimony of the other witnesses amply demonstrates the problems.

Eighteen months average pendency for patent applications is the PTO's overriding goal. Congress can help the PTO provide a superior and more prompt examination in biotechnology by directing the PTO to abandon this bean counter's tool showing apparent productivity at the expense of both quality and real productivity. Quality, not "eighteen months", should be the key policy goal. Shedding "eighteen months" would permit a more focused use of resources on biotechnology cases, and elimination of literally hundreds of Examiner positions in other technologies. A professional climate necessary to retain Examiners could be fostered.

The automated patent searching system known as "APS", patent rulemaking and legislation are three other important areas of concern, but secondary to ending "eighteen months".

House Committee on Small Business
Subcommittee on Regulation
and Business Opportunities

Biotechnology Patenting
Harold C. Wegner
March 29, 1988

THE ROOT PROBLEM: "EIGHTEEN MONTHS"

"Eighteen months" is the all-consuming goal of the PTO. It's the very evil that blocks an efficient examination of patent applications. If abolished, existing resources could be focused on a quality patent examination, and literally hundreds of Patent Examiner positions could be permitted to be quickly phased out.

Why? For most cases outside the area of biotechnology, the applicant would typically wish to defer examination for a considerable period of time. In the roughly no more than ten percent of cases where an applicant wants examination within the first year, he should be permitted to go to the front of the line. Otherwise, the case should sit.

The U.S. "instant examination" is particularly detrimental in the face of the multiphase system in Europe where there is first a prior art search at roughly 18 months, and commencement of examination six months later. As a result, the European examination "piggybacks" the U.S., instead of vice versa.

18 Months -- From When?

The good news -- The PTO is close to meeting its goal. The bad news -- The goal is nothing more than a bean counter's trick of no realistic positive meaning -- and with highly negative implications, particularly for biotechnology.

"Eighteen months". A term with two meanings. The rest of the world considers 18 months in the context of automatic

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publication of all patent applications 18 months from the first filing of any patent application to an invention.

(i) 18 Months -- the International Way

The international 18 month system started a generation ago in Holland in 1964, followed by Germany in 1968, Japan in 1971, and many European countries via the European Patent Convention of 1973, isolating America from almost all other countries. In 1987, Canada passed legislation to join the rest of the world.

Let's consider how the international system works when an American inventor, starting outside the "international system", files in several countries. For example, what happens when an inventor in Portland files a patent application for his invention in each of the United States and Japan? Eighteen months from the first filing, the Japanese Patent Office publishes the full text of the invention in Japanese. There is no U.S. publication--there is secrecy of the parallel U.S. application until grant of the patent. As a result, the Japanese R&D community gets the full text of the patent application at 18 months with its often rich detail of scientific information. In Japanese. The American researcher in a small enterprise without realistic, affordable access to Japanese publications is shut out until grant.

(ii) Eighteen Months the PTO Way

The PTO proclaims average pendency in 18 months. That sounds good. The question is: Eighteen months measured from when? Whereas the international system measures 18 months from

the earliest filing date of any application, the U.S. system measures 18 months only from the latest application in what may be a chain of replacement applications ("continuations").

What's the difference? A bookkeeping trick! An invention often is the subject of a series of patent applications. First one application is filed, and then replaced by a first continuation application, by another, and then perhaps still another. There is no limit.

The international system uses the intellectually more honest approach of judging pendency from the earliest filing date of any patent application in a series of cases. For example, if an application is filed in 1970 and then in 1985 is replaced by a "continuation", and granted in 1986, what is the pendency? In "real time", it's 16 years; "PTO-time" is one year.

When pendency is measured in "real time" -- not "PTO-time" -- the average pendency has been only very slightly dented in the past few years. Applicants are forced to file a greater number of continuations, so the PTO-time statistics improve.

In fact, the greater the number of continuations, the greater the inefficiency, the greater the real time for examination, the greater the cost to applicants -- and to taxpayers for such paper shuffling.

The Harm from the Simple Bookkeeping Trick

PTO preoccupation with the creation of an average pendency of 18 months from the latest in a chain of cases means that:

- Inventions are examined in the United States before the parallel European application, so that the U.S. Examiner does not have the benefit of the European Examiner's opinion on the parallel case when the U.S. Examiner first acts on a case.

- Patent applications seemingly in allowable form are suddenly subject to reconsideration, as late in the U.S. granting phase the European Examiner's parallel search results points to an error of omission in the U.S. proceeding.

- Examiners are encouraged to deny entry of amendments to patent applications, to force the applicant to refile a continuation (cutting the pendency for the case to the time starting with the continuation);

- Examiners are forced to act promptly on all cases, often as soon as they hit their desk -- even though the inventor may have no desire in such immediate treatment.

- A great overall inefficiency is built into a system where plural patent applications (continuations) are filed where one would suffice.

The inefficiency of the arbitrary 18 month average pendency goal strips the Examiner of the time needed to do his job properly. The circus atmosphere created by pushing paper as the number one goal drives quality Examiners quickly to the outside practicing bar -- particularly in biotechnology where new talent is in such scarce supply.

A USELESS COMPUTER SEARCHING SYSTEM

The idea of spending, literally, hundreds of millions of dollars on the PTO's new "APS" automated patent search system is mind boggling. That it is virtually useless to reliably search

for modern biotechnology inventions in the recombinant DNA field is even more mind boggling. But true.

There is supposedly "whole text" searching of patents in the APS system. That's the good news. But, a DNA fragment -- the heart of a biotechnology search -- is often set forth in a table or formula in the patent. The data base for the APS does not include such information! A whole text search by the APS system thus is totally useless as a reliable search tool when DNA fragments in tables are a necessary element of the search.

Even if a "perfect" whole text search system for patents were to be developed by the PTO, it would be defective for biotechnology because much (if not indeed most) of the pertinent recent prior art is in scientific literature outside the field of patents.

What can be done? The PTO would be well advised to reconsider its rush to put the APS on stream. Perhaps in some "Widget" arts remote from biotechnology, there may be motivation to continue with APS. In the field of biotechnology -- as well as organic chemistry and pharmaceuticals -- a better investment would be to work with existing services such as provided by Chemical Abstracts.

RULEMAKING - THE INTERNAL PRIORITY DOCUMENT (IPD)

At least as serious as "eighteen months" and the APS problems are the competitive disadvantages American industry faces by the absence of an "Internal Priority Document" (IPD) system. Japan, Germany and most of Europe have a formal or

informal IPD system; America does not. What is an IPD, and what are the consequences to American biotechnology by the PTO's failure to have implemented such a system?

An "Internal Priority Document" (IPD) is a simple patent application. Like a regular application, it contains the "guts" of the invention, but has few formalities and typically a fee of roughly $25.00 to $100.00. The IPD is "stamped in" to the local patent office, and is replaced within one year by a more normal patent application. That later, "normal" patent application is dated back to the IPD filing date.

The IPD - A Race to the Courthouse Priority Ticket

It is crucial that an American biotechnology enterprise obtain the earliest filing date for a new invention. The implications are truly global, because an American's rights in Japan, Germany, France, Great Britain and every other major country outside North America are keyed to this earliest filing date. (The foreign application filed within one year of that date is "dated back" to the earliest filing date.)

Americans lack an IPD system. Americans often delay weeks or months in filing their U.S. application, their worldwide priority date. Consider the following situation:

- On January 1, 1988, American Biowidget conceives a new biotechnology invention. The American company needs three months to obtain funding to start working on the project, and then takes ten weeks to file the first case in the United States, receiving a filing date of June 15, 1988. Only later is the proof obtained that the invention works ("reduced to practice").

- On May 1, 1988, Kyoto Biowidget independently creates the identical invention, and "stamps in" an IPD in Tokyo on June 1, 1988, with a full disclosure of the invention.

- On June 1, 1989, Kyoto Biowidget files a United States application, claiming priority based on its Japanese IPD.

In this scenario, Kyoto Biowidget has a date of invention for both the United States and Japan of May 1, 1988. In Japan (as well as all important countries of Europe and, shortly, Canada), Kyoto Widget automatically has priority: "First to file" in the rest of the world makes the actual invention date meaningless as between two independent inventors.

Even in the United States, Kyoto Widget should win the patent. Proving a mere conception of an invention is a meaningless act for real world situations. Periods of laboratory inactivity due to a search for financing generally kills reliance on a mere conception date.

Even without the funding problem, Kyoto Biowidget stands in the position of "senior party" in the United States. This means that the American -- the "junior party", must prove that he actually made the invention at an early date through contemporaneous evidence. This difficult feat results in the junior party often giving up, winning less than about one in four priority contests ("patent interferences"). If the lack of evidence doesn't kill the junior party, the often six figure legal bill that a junior party faces will be the death blow: What financial expert is willing to bankroll a one in four chance with two to five years of uncertainty in the final outcome--

with the three in four result of a loss meaning that the opponent can ultimately obtain an injunction to shut down the junior party?

Rulemaking

No statutory change is necessary to implement an IPD system: Congress already provided the necessary legislation in 1982, Public Law 97-247 (1982), that permits the Commissioner to create the IPD system.

LEGISLATION

Comprehensive patent legislation is also necessary. Until recently, the United States and Canada were the only two major countries to lack the "international system" -- first to file, fixed term from the filing date, automatic publication at 18 months, and several other related features.

Less than a year ago, Canada passed legislation to join Europe and Japan -- isolating the United States as the only major country of the world with the "old" system.

Old is not necessarily bad. Indeed, many of the cherished principles of American patent law have been incorporated into the international system. But, with both Europe and Japan having overhauled their patent laws in the past generation -- and Canada just this past year -- it is fundamental that the United States join the rest of the world.

Failure to modernize has its domestic costs and inefficiencies. That, alone, may be tolerable. What makes our failure to modernize and harmonize our system completely unacceptable is the gross competitive disadvantage that American industry faces in Japan and Europe. Americans routinely lose their Japanese and European patent rights.

If the three major patent granting authorities in Tokyo, Munich and Crystal City had a truly harmonized system, ultimately preliminary prosecution could be had in only one of the three offices -- cutting the costs for initial searching and examination to one third for both applicants and taxpayers alike. My views are more fully expressed in a paper, "Patent Law Simplification and the Geneva Patent Convention", 14 AIPLA Q. J. 154 (1986).

Mr. Chairman, and Members of this Committee, I again thank you for the opportunity to express my views on this important topic. You are to be commended for your interest and leadership in a complicated but very important problem for small biotechnology enterprises.

# # #

Statement of William Hostetler
Before the
Sub-Committee on Regulation and Business Opportunity
of the
Small Business Committee
United States House of Representatives

I am William Hostetler, Director of Technology Transfer at Oregon State University, Corvallis, Oregon, and Western Region Vice President for the Society of University Patent Administrators (SUPA).

The slow processing of biotechnology patent applications is a major concern for universities involved in research and the licensing of technology. Our experience has shown that it takes approximately 28 months to receive a first action from the patent examiner in biotechnology. Washington State University filed a patent application pertaining to the sequencing and expressing of the recombinant bovine IL-2 gene (patent pending #862,812) on May 13, 1986. They are still waiting for the first office action. This technology has not been licensed because companies are holding back in negotiations until the university can show that there is a possibility of achieving patent protection. Meanwhile, industrial researchers have sequenced the IL-2 gene and are proceeding with commercialization.

The delay in receiving a first office action can create problems for universities that are considering filing foreign patents. In most foreign countries, applicants have one year from the date of the U.S. filing to receive benefit of the United States filing date. The expense of foreign filings is high, and it is desireable to have the initial opinion of the patent examiner before deciding whether to file. With the slow response time in the biotechnology area, universities often commit substantial funds in foreign patent filings before receiving information from the United States Patent Office that protection is unlikely.

Universities, especially public institutions, have historically required researchers to publish. The number and quality of publications weigh heavily in the tenure and promotion process. State right-to-know laws make it difficult for a state institution to maintain trade secrets. In many instances, enabling publications concerning patentable technology is in print very soon after a patent application has been filed. There have been instances of companies having marketable products on sale based on information derived from academic researchers' publications long before the institution has received the first action from the patent office.

Many of the examiners in the biotechnology field are inexperienced and tend to cite prior art and technical objections in the first office action rather than addressing the issue of

patentability and the merits of the claim in the patent. I was told of an instance where a patent attorney responded to the first action with testimony from four expert witnesses answering the question of obviousness and received a response from the examiner simply stating claims denied based on reasons of record. The response did not address the issues raised by the witnesses or explain which reasons of record hadn't been addressed.

Most examiners in the biotechnology area tend to respond negatively to the inventors. Rather than taking the time to understand the substance of the application and helping the inventor receive patent protection, the examiners respond to minor technicalities and make the patent process a costly, time consuming experience for the inventor.

The cost of receiving patent protection is a major concern to universities, most of whom utilize private patenting firms. The cost of receiving a United States patent in most fields runs between $3,000 and $6,000. However, the biotechnology patents cost between $8,000 and $15,000. This cost differential is primarily due to attorney fees and the time factor involved responding to technicalities, and in a sense, educating the examiner concerning the specific biotechnology and how it is different from existing biotechnology.

State governments and industry are pressuring universities to identify and expediently move technology into the marketplace. The major research universities in the United States are a primary source of new discoveries in the biotechnology field. Most major research universities have created technology transfer offices or foundations to encourage researchers to look for patentable concepts in their research, and then patent and license the technology brought forward.

The researcher, whose primary duties are to educate students and conduct research, is the person who, if he/she discloses a new invention, must spend a great deal of time responding to the patent attorney who in turn spends time and money educating the examiner. Many researchers are involved in new research before we receive a first action from the patent office and are hesitant to spend a great deal of time explaining research that occurred two and one-half or three years ago. This creates an atmosphere where many researchers are hesitant to bring their ideas forward. Perhaps it would be beneficial to have examiners visit industries or universities as an education process. If they have a greater understanding of what is happening in the labs, it might speed up the patenting process.

It has been suggested that if an inventor desires to speed up the patent process they can file an application to make special. The application is then marked to receive special

consideration over other patents that are not marked to receive special consideration. This process may speed up an individual application, but it does not solve the problems of an area that is overloaded like the biotechnology area.

I have been told that patent examiners in the biotechnology area have unwritten standards that they are utilizing. If these standards are formalized and shared it would enable the attorneys to draft patent applications that address these standards, and thus, there would be less office actions. With less office actions, the patent process should take less time.

In closing, I have a few suggestions that should speed up the patent process.

1. Increase the time allowed for an examiner to spend on a specific case. If the application has 122 claims, it will normally take more time to review and understand than a case with 10 or 15 claims. Encourage the examiners to go to the substance of the application rather than formalities on the first office action.

2. Provide the examiners with adequate support staff, thus enabling the examiners to spend their time reviewing the applications.

3. Be consistent on the kinds of claims allowed and standardize the criteria on claim scope. This will enable patent attorneys to prepare applications that should move more swiftly through the process, thus decreasing the backlog.

4. Each case in the biotechnology field is highly specialized. It might be beneficial to have the examiners be encouraged to discuss the technology with the inventor early in the application process, thus giving the examiner more understanding of the technology. Encourage the examiner to visit industry or research labs as an educational tool.

5. Examiners in the biotechnology field must be highly knowledgeable individuals. Their skills are in demand in research labs and law firms, as well as the U.S. Patent Office. To hire and maintain these individuals, the salary, benefits, support staff, and other working conditions must be competitive.

The patent office has become more efficient over the last few years. The computerization of records and the concept of a paperless office should continue to increase the efficiency. The biotechnology area may tend to be self correcting over time as

the examiners become more experienced. The patent office must allocate additional revenue sources for the biotechnology field and allow the biotechnology section to compensate examiners on a competitive basis, then we will begin to see more experienced examiners in biotechnology.

Thank you Mister Chairman

There is one additional item that I would like to address as an addendum to my testimony. It is an issue that causes problems for universities in licensing to small biotechnology firms. The cost of Product Liability Insurance for small biotechnology companies is so high that most of them are forced to proceed without liability protection. Many universities are hesitant to license technology to a company that does not have liability insurance. If a small biotechnology company were to incur liability without protection, there is a strong likelihood that the universities' endowment would be a prime target. This creates a roadblock in the flow of biotechnology from universities to small companies, and small biotechnology companies should be encouraged to help in the creation of new jobs and bolstering the economy. Perhaps this Sub-Committee on Regulation and Business Opportunities could address this issue at a later date.

DR. PHILIP CARTER

BIOTECHNOLOGY PATENTING

PROBLEMS AND SOLUTIONS

A White Paper

North Carolina State University
Research Administration

March 25, 1988

The question is whether there is a problem because of the backlog of applications in the United States Patent and Trademark Office in the field of biochemistry and biotechnology and the long delay in getting initial actions on those applications and having patents issued. The answer is that it clearly is a problem and one that needs attention.

Problems Created by the Backlog

From the university standpoint the problem appears in several areas. The first is that the delay in having a patent issued can slow down efforts to license an invention or to sell the invention or get it into commercial use where it will benefit the public. Frequently potential licensees or users of the invention are hesitant to invest the money, resources, equipment, and people that are necessary to take an invention from the laboratory or research stage at the university to do further development and get it into the marketplace unless they are assured that they will have patent protection to give them the right to exclude others from copying.

A second problem has to do with filing for protection in foreign countries. Under United States law, an applicant having filed in the United States has one year within which to file in foreign countries and, under the Paris convention, obtain the benefit of the United States filing date. Customarily, this decision is postponed until near the end of the first year because of the considerable expense of foreign filing. In practice, it is highly desirable to have the search made by the United States Patent Examiner and his initial opinion prior to that one year period so that the patent applicant

would have the benefit of that initial Patent Office search and reaction before making the decision regarding spending the money for foreign filing. Without that action by the U.S. Patent Office the decision is much more difficult and sometimes involves committing substantial funds when patent protection is not likely.

There is a problem arising from the fact that pending patent applications are secret. Thus when an inventor has an invention and he makes a preliminary search to try to determine if his invention is novel and patentable, he has no access to the backlog of pending applications which are on file in Washington. Therefore, there is a stronger likelihood that the inventor will proceed with an application believing it to be new and patentable, and later be subject to having his application rejected when an application that had been pending later issues. Once a patent issues, it in effect relates back to its early filing date. The result is a considerable body of hidden prior art that creates potential jeopardy to the inventor.

Another aspect of the large body of secret pending applications is the fact that one of those applications may issue as a dominating patent which will have claims in it broad enough to encompass the use of a later invention and create problems with infringement. The greater the backlog of pending applications in the Patent Office, the greater the likelihood of a dominating patent issuing which could create problems for an inventor who has proceeded in good faith, believing that his invention is novel, and relying upon his patent application to get started in commercial use.

Another problem relates to the quality of applications which are being issued as patents. There is a continuing problem of patents issuing which should not have issued if the examiners were properly qualified and properly advised of the prior art and procedures in industry. Therefore, caution should be taken that any effort to speed up the examination proceeding does not result in reduced quality or the issuance of patents of doubtful validity.

Past Suggested Solutions

One suggested solution is to adopt the Japanese procedure of allowing the patent application to have only a single claim so that each patent application would be very narrow, rather than having a full disclosure and a range of claims for broad scope. This proposal has serious drawbacks. In Japan they do generally require a very narrow scope of each patent and only a single claim. However, in Japan the subsequent interpretation of that claim is treated very broadly and the Japanese permit very wide expansion and broadening of the original disclosure. The United States requires a more comprehensive disclosure, one which is adequate to disclose the invention and teach someone of ordinary skill in the art how to practice it. For worthwhile inventions it is possible to obtain broad protection which would cover, for example, a formula and a product and a method of making it all in a single application. This makes it a much more valuable property right for licensing and use.

The danger is where the examiner issues a patent that is too broad in view of prior art. This has to do with the examiner's expertise rather than any change in the law. It would be a great mistake to go to a system where each application and each patent would be very narrow and limited. That would have a very adverse effect upon the value of the property rights of the patent.

Another proposal is to adopt a system of filing an internal priority document, which would have the effect of being a patent application, and could be relied upon to establish a date of invention under the international convention. Again, this procedure is insufficient. There is now a provision in the United States law where an application can be filed with an initial disclosure which should be sufficient to meet the requirement of the law in being a complete disclosure. Even if this is fairly narrow, under the law, a continuation-in-part application may be filed later. Therefore, there is already in place the provision for filing an application at an early stage, obtaining a date, and then later enlarging that application if circumstances require. To permit the filing of insufficient disclosures that do not adequately disclose and teach the invention is not an appropriate solution.

The next proposal is to adopt a first to file system which in effect says that the patent goes to the first one who files for it in the Patent Office rather than to the first inventor. Aside from whatever constitutional problems this may present, it creates a very real burden on the small inventor and on the universities. The small business that has limited money frequently needs some time period to

evaluate the invention, test it, and explore the commercial market before investing in the cost of a patent application. This is particularly true in the university environment where the commercial prospects for an invention must be evaluated before spending the very limited funds which are available for patent protection. So the first to file system would not reduce the backlog of patent applications. All it would do would be to eliminate interference proceedings in the Patent Office, and it does not appear that interference proceedings or contests as to the priority of invention are a major factor in slowing down the grant of patents.

A one year grace period, which is a key provision of the law, is absolutely critical for the small business, individual inventor and the university research area. Most provisions that talk about going to a first to file system effectively eliminate that grace period. Even though there have been proposals to combine the two, the details have not been worked out. The grace period is needed particularly in the university because of the desire for university professors to publish. Once they publish a complete disclosure of their invention, or even an abstract which might teach the invention, they have one year in which to file a patent application. Because of the propensity for professors to rush the publication, it frequently happens that they publish before they disclose the invention to the appropriate patent administration for consideration in filing. So this time period is very important. It was noted that the university has limited funds and usually needs to do some testing and exploring

of commercial market and potential licensees before filing a patent application and the one year grace period is just absolutely essential in the university environment.

Another proposal that has been put forth would be to split the filing and examination fees. An alternative would be to provide for the payment of an extry fee to obtain an expedited examination in the Patent Office. This proposal would solve the problem for those inventors who need a prompt decision as to whether the application is patentable before proceeding with commercialization. However, it would tend to benefit those with the deep pockets more and it would not solve the overall problem of the backlog of patent applications. It could be expected that the examining force would examine some of these applications out of order. The result would be that the great bulk of the applications would continue to be waiting and the backlog would increase. Thus the problem of hidden prior art would still exist.

Another proposal is to have applications published within 18 months after filing. This proposal has some merit in that it would reduce the problem of hidden or secret prior art because any application would become published after 18 months and people searching or concerned about infringement issues would have that art available. The biggest drawback to this is the fairly common procedure utilized in this country, and particularly in the university and biochemistry environment, that is, it is often

recommended practice to file an application as quickly as possible on a given species or formula or invention knowing that further research or development will broaden the scope of that invention. So an initial application is filed that has a fairly narrow disclosure, and after further work is done, a continuation in part application is filed adding the additional data and broadening the scope of the disclosure and the scope of claimed protection. If that initial application is published after 18 months, it could frequently lead to spurring others on to work in this area, and perhaps limit the benefits of the natural progressive research in a particular area. While the 18 month publication provision has some merit, it also has some downside aspects with respect to continuing research. Changing the life of the patent to run from 20 years of the filing date instead of 17 years from the issue date would conform to practice in many other countries. However, this would not help alleviate the backlog of applications awaiting examination. As long as there is a backlog of applications, the net result could be that the life of the patent would be reduced instead of extended. For example, if it takes five years to get through the Patent Office, the life of the patent would only be 15 years instead of the present 17 years from the date of issue.

New Proposed Solutions

One solution would be better and more efficient use of the experienced examiners in the Patent Office. Steps are already underway, or perhaps even been accomplished, to reorganize the

examining group in the Patent Office in order to put all the examiners who have capability in the biotechnology area into one group and to arrange the work load so that they are working only in this area and are not loaded down with work which other examiners could do.

A key solution is to provide better compensation for examiners, particularly those examiners in the biochemistry/ biotechnology area. This is a newly developing area of technology; there are not many individuals who meet the requirements. There is a very large, competitive demand for skilled people in this area. If the Patent Office is to acquire skilled examiners who are knowledgeable in the area, they need to provide more adequate compensation and perhaps cut through some of the red tape and bureaucratic rules with respect to hiring.

One aspect of this is that present requirements call for a Ph.D. plus postdoctoral experience. This much experience is not necessary for a qualified examiner; there are many Bachelor programs in universities which would provide a 4 year training course resulting in highly qualified people who should have the basic qualifications to be good examiners in this area. One of those programs is available at North Carolina State University. This would not only help the Patent Office, it could open up additional job opportunities.

Another problem is that most of the relevant prior art in the biochemistry/biotechnology field is not found in prior patents. The art is new and rapidly developing and most of the art will be found in technical publications and literature. One solution would be to provide ways and means to make this other art clearly available to the examiners and to give them facilities for adequately searching that art. For example, they should have computer search facilities that would give them access to the many research libraries around the country and where this type of art is found.

Another way to improve the quality of the examiners would be to increase private sector education. For example, the examiners could be encouraged to visit some of the research universities and gain firsthand experience as to what is taking place in the real world and the problems and difficulties in procedures that are faced by research scientists in the biotechnology field. This would give the examiners a much better understanding of these developments and the problems involved as well as the thrust of current developments and research.

From the standpoint of goals, it would be most helpful to have the first action by the United States Patent Office and the examiners search results within 10 months of the filing date. This would give the inventor some indication as to the scope of patent he was likely to get or not get, the most pertinent art found by the examiner, and would be very helpful in determining whether to spend the money on

foreign applications and how much money should be committed in further research and commercialization. The second goal would be to have the actual patent issue within 2 years. Those would be highly desirable goals.

ADDRESS

TO THE

INDUSTRIAL BIOTECHNOLOGY ASSOCIATION

LOOKING TO THE FUTURE: PLANS AND PRIORITIES

OF THE U.S. PATENT AND TRADEMARK OFFICE

BY

DONALD J. QUIGG

ASSISTANT SECRETARY AND

COMMISSIONER OF PATENTS AND TRADEMARKS

OCTOBER 22, 1987

OF ALL THE TECHNOLOGIES ENCOMPASSED BY PRACTICE BEFORE THE PATENT AND TRADEMARK OFFICE, NONE IS FASTER-GROWING, NONE IS MORE EXCITING, AND NONE HOLDS A GREATER PROMISE OF BENEFIT TO MANKIND THAN BIOTECHNOLOGY. MY JOB AS COMMISSIONER IS TO SEE THAT THE PATENT SYSTEM CONTINUES TO ENCOURAGE NEW TECHNOLOGY AND THAT IT DOES NOT GET IN ITS WAY.

ALONG THE PATHWAY BETWEEN INVENTIVE CONCEPTION AND COMMERCIALIZATION, THE PATENT SYSTEM HAS THE POTENTIAL FOR BEING EITHER A BRIDGE OR A ROADBLOCK. WE WANT TO ENSURE THAT ALL LANES REMAIN CLEAR, EVEN IF THAT MEANS PLACING MYSELF IN THE MIDST OF A GREAT NATIONAL ETHICS DEBATE (AS IN THE CASE OF ANIMAL PATENTING.) I PLAN TO TALK ABOUT THAT DEBATE, AND HOW IT CAME ABOUT.

I ALSO WANT TO TALK ABOUT THE RELATIONSHIP OF THE U.S. PATENT SYSTEM AND THE BIOTECHNOLOGY INDUSTRY — AND ABOUT PLANS AND PRIORITIES AT THE PTO WHICH SHOULD HAVE IMPACT ON THAT INDUSTRY IN THE COMING YEARS.

I WAS CAUTIONED THAT MANY IN THIS AUDIENCE MIGHT KNOW LITTLE, IF ANYTHING, ABOUT THE SUBJECT OF PATENTS. I THINK IT IS ALSO SAFE TO SAY THAT MANY OF US (MYSELF INCLUDED) ARE ESSENTIALLY "BIOTECH-ILLITERATE." HOWEVER, THIS WILL BE NEITHER THE FIRST NOR THE LAST WASHINGTON MEETING WHERE <u>NO ONE</u> UNDERSTANDS WHAT <u>ANYONE</u> IS SAYING!

LET ME START BY EXPLAINING IN VERY GENERAL TERMS JUST WHAT THE PATENT SYSTEM IS ABOUT. THE CONCEPT OF REWARDING INVENTORS AND AUTHORS WITH EXCLUSIVE RIGHTS TO THEIR WORKS IS CENTURIES OLD. THE

FRAMERS OF AMERICA'S CONSTITUTION, IN FACT, ADOPTED THIS GENERAL CONCEPT AND REFINED IT WITHIN ARTICLE I, SECTION 8, CLAUSE 8, TO REFLECT THE INTRINSIC RIGHT OF THE PEOPLE TO THEIR RESPECTIVE DISCOVERIES AND WRITINGS. TO "PROMOTE THE PROGRESS OF SCIENCE AND USEFUL ARTS,"[1] THE U.S. CONSTITUTION GIVES CONGRESS POWER TO SECURE THAT EXCLUSIVE RIGHT FOR A LIMITED PERIOD OF TIME. UNDERSCORE THE TERM "EXCLUSIVE." IN A MOMENT WE WILL SEE HOW SIGNIFICANT THAT TERM IS IN THE GENETIC ENGINEERING FIELD.

THE PATENT SYSTEM PROMOTES PROGRESS OF SCIENCE AND USEFUL ARTS IN AT LEAST TWO PRINCIPAL WAYS. THE FIRST HAS TO DO WITH THE LIMITED EXCLUSIVITY TO THE INVENTED TECHNOLOGY WHICH IS CONVEYED TO THE PATENT OWNER THROUGH THE PATENT GRANT. BY THIS I MEAN THAT FOR A LIMITED PERIOD OF TIME (17 YEARS) A PATENTEE HAS THE RIGHT TO EXCLUDE OTHERS FROM MAKING, USING, OR SELLING THE INVENTION. THIS PRESENTS INVESTMENT SECURITY FOR THOSE WHO PLACE VALUABLE RESOURCES INTO THE OTHERWISE RISKY PROCESS OF RESEARCH, NEW PRODUCT DEVELOPMENT, AND COMMERCIALIZATION.

A SECOND WAY THAT THE PATENT SYSTEM PROMOTES PROGRESS IS IN ITS ROLE AS A POWERFUL GENERATOR OF INFORMATION. TO OBTAIN A PATENT, AN INVENTOR MUST PRESENT A FULL DISCLOSURE OF THE INVENTION. SOME REFER TO THIS AS THE "CONTRACT THEORY" OF PATENT LAW. IT IS SORT OF A QUID PRO QUO — DISCLOSURE OF THE FULL DETAILS OF THE NEW TECHNOLOGY IN EXCHANGE FOR ITS TEMPORARY EXCLUSIVE CONTROL. HERE, UNDERSCORE THE TERM "DISCLOSURE." THROUGHOUT THE WORLD, MORE THAN A QUARTER MILLION UNIQUE INVENTIONS ARE PATENTED EACH YEAR. YOU CAN IMAGINE WHAT A

WELLSPRING OF NEW KNOWLEDGE THEY WILL PROVIDE TO FUTURE INVENTORS.

SPEAKING OF THE HIGH LEVEL OF PATENTING ACTIVITY, I BROUGHT ALONG A RECENT PTO REPORT[2] WHICH REVIEWS PATENTING STATISTICS IN THE FIELD OF GENETIC ENGINEERING. THE INFORMATION WAS GENERATED FROM OUR TECHNOLOGY ASSESSMENT AND FORECAST DATABASE, AND COVERS A TIME PERIOD FROM 1963-1986. (IF YOU WISH, YOU CAN PICK UP A COPY AT THE END OF THIS SESSION.) THE REPORT FOLLOWS THE U.S. PATENTING TRENDS OF MORE THAN 200 CORPORATIONS AND UNIVERSITIES IN 21 COUNTRIES. IT IS BASED UPON A COLLECTION OF ALL THE PATENTS WE COULD FIND INVOLVING GENETIC ENGINEERING TECHNOLOGY -- EVEN THOSE GRANTED AT THE EARLY FRINGES OF THE NEW SCIENCE. THE REPORT GRAPHICALLY REFLECTS THE EXPLOSIVE RISE OF U.S. PATENT ACTIVITY IN GENETIC ENGINEERING. HOWEVER, I FOUND THE CHANGING RATIO OF U.S. AND FOREIGN INVENTOR ACTIVITY TO BE A BIT SURPRISING; PARTICULARLY IN VIEW OF THE HEAVY FOREIGN ACTIVITY WE HAVE SEEN IN OTHER TECHNICAL AREAS.

FOR GENETIC ENGINEERING INVENTIONS, THE NUMBER OF U.S. PATENTS ISSUED TO U.S. RESIDENTS DURING THE YEARS 1963-1980 TOTALED 48, WHILE FOREIGN RESIDENTS RECEIVED 64. SINCE 1980, HOWEVER, THE BALANCE SHIFTED DRAMATICALLY. FROM 1981 THROUGH 1986, U.S. RESIDENTS RECEIVED 347 U.S. PATENTS AS COMPARED TO 136 FOR FOREIGNERS. THAT IS A HEARTWARMING TURNAROUND! WHILE 116 U.S. PATENTS WERE GRANTED LAST YEAR IN THE GENETIC ENGINEERING FIELD, FOREIGNERS RECEIVED ONLY 22% (WITH HALF OF THAT ACTIVITY FROM JAPAN). COMPARE THAT TO THE 46% FOREIGN SHARE OF ALL U.S. PATENTS GRANTED LAST YEAR!

GENETIC ENGINEERING, OF COURSE, IS NOT THE ONLY BIOTECH AREA WHERE INNOVATION IS ON THE RISE WHILE THE FOREIGN SHARE IS DECREASING.

ACCORDING TO ANOTHER RECENT U.S. PATENT ACTIVITY REPORT[3], PATENTING IN THE AREA OF MOLECULAR BIOLOGY AND MICROBIOLOGY INCREASED FROM 358 U.S. PATENT GRANTS JUST 8 YEARS AGO TO 780 GRANTS IN 1986. HERE AGAIN, THE PERCENTAGE OF FOREIGN INVENTORS DECLINED (FROM 44% DOWN TO 42%).

SO, THE U.S. PATENTING RATES IN YOUR FIELDS ARE RELATIVELY HIGH AND PREDOMINATELY OF U.S. ORIGIN. THIS IS A HEALTHY SIGN FOR YOUR INDUSTRY, PARTICULARLY WITH RESPECT TO FOREIGN COMPETITION. I WOULD LIKE TO THINK THAT THIS ALSO REFLECTS A MEASURE OF CONFIDENCE YOUR INDUSTRY IS PLACING IN THE U.S. PATENT SYSTEM — DESPITE A NUMBER OF PROBLEMS (OR, AS I WOULD CALL THEM, "OPPORTUNITIES FOR CREATIVE THINKING").

IN THE TIME REMAINING, I WANT TO ADDRESS SOME OF THOSE "OPPORTUNITIES," BUT FIRST LET ME TELL YOU ABOUT THE GREAT NATIONAL ETHICS DEBATE.

ONE OF THE "HOTTEST" ISSUES OF THE YEAR FOR THE PTO IN THE BIOTECH AREA (OR ANY AREA FOR THAT MATTER) HAS INVOLVED OUR POLICY STATEMENT CONCERNING THE PATENTING OF ANIMALS. CRITICS REALLY CAME OUT OF THE WOODWORK ON THAT ONE. THE MEDIA PEOPLE HAVE HAD A FIELD DAY. THE CONGRESS HAS HELD SEVERAL PUBLIC HEARINGS, AND HAS SUGGESTED SOME RATHER DISTURBING LEGISLATION. LET ME TAKE A COUPLE OF MINUTES TO TELL YOU HOW THAT POLICY DECISION CAME ABOUT, AND JUST WHERE THE PTO STANDS ON THE MATTER OF ANIMAL PATENTING.

THE POLICY STATEMENT ON ANIMAL PATENTING WAS NOT "SPUR-OF-THE MOMENT," AND THE THINKING BEHIND IT WAS NOT DONE IN A VACUUM. MANY OF THE BEST LEGAL AND TECHNICAL MINDS IN THIS COUNTRY HAD BEEN STRUGGLING WITH THE ISSUE FOR A LONG TIME.

IN 1975, WE ALMOST HAD THE ISSUE RESOLVED FOR US IN A COURT CASE CALLED IN RE MERAT[4] INVOLVING A "DWARF HEN." THAT'S A "SUBNORMAL SIZED CHICKEN." HOWEVER, THE PATENT GRANT ON A LIVING CHICKEN WAS REFUSED ON OTHER GROUNDS.

IT WAS NOT LONG BEFORE IT RAISED ITS HEAD ONCE MORE (THE ISSUE NOT THE CHICKEN!). THE 1977 DECISION BY THE COURT IN IN RE BERGY[5] INVOLVED A BIOLOGICALLY PURE CULTURE OF MICROORGANISM CAPABLE OF PRODUCING AN ANTIBIOTIC. AT THE TIME, THE PTO HAD HELD THAT THIS CULTURE WAS NOT PATENTABLE SUBJECT MATTER SINCE IT WAS ALIVE. THE COURT CONCLUDED THAT THE MERE FACT THAT THE SUBSTANCE SOUGHT TO BE PATENTED IS ALIVE DOES NOT REMOVE IT FROM THE CATEGORIES OF THINGS THAT CAN BE PATENTED. INTERESTINGLY, THE COURT WENT ON TO NOTE THAT THE CLAIMED MICROORGANISM ARE MORE AKIN TO INANIMATE CHEMICAL COMPOSITIONS SUCH AS REACTANTS, REAGENTS, AND CATALYSTS THAN THEY ARE TO HORSES AND HONEYBEES OR RASPBERRIES AND ROSES.

SO, A GREAT DEAL OF THOUGHT HAD GONE INTO THIS ISSUE OF PATENTING LIFE FORMS. UP UNTIL THE 1980 SUPREME COURT RULING IN DIAMOND V. CHAKRABARTY,[6] THE PTO TOOK A FIRM POSITION ON THE MATTER. THE PTO MAINTAINED THAT ANY LIFE FORM, EVEN A SINGLE CELL ORGANISM, WAS NOT PATENTABLE SUBJECT MATTER UNDER U.S. LAW. ONLY LEGISLATIVE ACTION, THE PTO CONTENDED, WOULD PERMIT ENLARGING THE SCOPE OF PATENT PROTECTION TO COVER LIFE FORMS. MEANWHILE, GENERAL ELECTRIC CORPORATION RESEARCHER ANANDA CHAKRABARTY'S PATENT APPLICATION ON OIL-EATING MICROBES WAS MAKING ITS WAY THROUGH THE SYSTEM.

THE QUESTION BEFORE US IN CHAKRABARTY, SIMPLY STATED, WAS THIS: DOES A GENETICALLY ENGINEERED MICROORGANISM QUALIFY AS PATENTABLE SUBJECT MATTER? THE PATENT EXAMINING STAFF, FOLLOWING POLICY BASED UPON THE CONTROLLING PRECEDENTS OF CASE LAW ANSWERED "NO." CHAKRABARTY APPEALED TO OUR INTERNAL TRIBUNAL, THE BOARD OF PATENT APPEALS AND INTERFERENCES -- THEY ALSO ANSWERED "NO." FINALLY, THE SUPREME COURT, IN A 5-4 DECISION, HELD THAT THE MAN-MADE MICROBES ARE INDEED PATENTABLE SUBJECT MATTER.

THE COURT STATED FLATLY THAT THE INTENT OF CONGRESS WAS THAT PATENTABLE SUBJECT MATTER INCLUDE "ANYTHING UNDER THE SUN THAT IS MADE BY MAN." THEY MADE THE FOLLOWING DISTINCTION. THE QUESTION OF WHETHER THE INVENTION "LIVES" IS NOT RELEVANT TO THE PATENTABILITY ISSUE. WHAT IS RELEVANT IS WHETHER THE LIVING THING IS THE RESULT OF HUMAN INTERVENTION.

AND, SO, IT WAS AGAINST THIS BACKGROUND THAT THE PTO WAS TO CONSIDER THE PATENTABILITY OF A POLYPLOID PACIFIC OYSTER. IN EX PARTE ALLEN,[7] THE EXAMINER REFUSED TO GRANT THE PATENT ON TWO GROUNDS: (1) THAT THE OYSTER PRODUCT WAS AN OBVIOUS VARIATION OF KNOWN POLYPLOID OYSTERS, AND (2) THAT MULTICELLULAR LIVING ORGANISMS ARE NOT COVERED BY U.S. PATENT LAW. APPLICANTS APPEALED. IN APRIL OF THIS YEAR, THE PTO APPEAL BOARD AGREED WITH THE EXAMINER'S REJECTION BASED ON THE POINT OF OBVIOUSNESS. AT THE SAME TIME, THE BOARD OVERRULED THE EXAMINER ON THE SECOND GROUND IN LIGHT OF THE REASONING WHICH HAD BEEN SET FORTH BY THE SUPREME COURT. WHILE THE DECISION DID NOT RESULT IN A GENERATION OF PATENTED CREATURES, IT DID RESULT IN AN AFFIRMATIVE

ANSWER TO THE THRESHOLD LEGAL QUESTION OF THE PATENTABILITY OF HIGHER LIFE FORMS UNDER THE GENERAL PATENT LAW. THE DECISION REACHES FAR BEYOND THE OYSTER BEDS ... TO THE ENTIRE ANIMAL KINGDOM ... STOPPING SHORT, I MIGHT ADD, OF THE PATENTING OF HUMANS.

ON APRIL 21ST, WE ANNOUNCED OUR INTERPRETATION OF THIS DECISION. THE PTO NOW CONSIDERS NON-NATURALLY OCCURRING, NON-HUMAN, MULTICELLULAR LIVING ORGANISMS, INCLUDING ANIMALS, TO BE PATENTABLE SUBJECT MATTER INSOFAR AS OUR PATENT STATUES ARE CONCERNED.

(WITHIN HOURS OF OUR POLICY ANNOUNCEMENT, YOU MAY HAVE SEEN ME BEING GRILLED REPEATEDLY ON THE NATIONAL NEWS — SHARING AIRTIME WITH AN EXPERIMENTAL, GENE-ALTERED ARTHRITIC PIG — WHILE COMMENTATORS AND HUMANE SOCIETY SPOKESMEN CHALLENGED ME TO DEFEND THE PTO POLICY. BELIEVE ME, THE PIG GOT MORE SYMPATHY.)

TO THOSE WHO HAVE FOLLOWED DEVELOPMENTS IN BIOTECHNOLOGY AND THE LAW, OUR POLICY ON PATENTING OF ANIMALS CAME AS NO SURPRISE. THE HUMANE SOCIETY AND OTHER ANIMAL-RIGHTS ADVOCATES, ON THE OTHER HAND, SUDDENLY FOUND A "CAUSE." NOTWITHSTANDING THE FACT THAT <u>OTHER</u> AGENCIES REGULATE ACTUAL PRODUCTION AND USE IN THIS AREA, THEY CHARGED THE PTO WITH MISTREATMENT OF HELPLESS ANIMALS. THEY SAID WE ARE HELPING TO CREATE BREEDING MONOPOLIES. AND THEY SAID THAT WE ARE "PLAYING GOD." A NUMBER OF CONGRESSMEN HAVE SOUGHT A MORATORIUM ON THE GRANT OF ANIMAL PATENTS.

I WOULD SAY THAT THE FOCUS OF ALL THE CONFLICT IS CLEARLY MISPLACED — THE ISSUE IS ONE INVOLVING ETHICS AND REGULATION, <u>NOT</u> QUESTIONS OF PATENT LAW. LET ME HIGHLIGHT AN IMPORTANT DISTINCTION.

YOU MAY RECALL MY SAYING THAT THE PATENT GRANT CONVEYS TO THE PATENTEE THE RIGHT TO EXCLUDE OTHERS FROM MAKING, USING, OR SELLING THE INVENTION. (REMEMBER WHEN WE UNDERSCORED THE TERM EXCLUSIVE?) THE "RIGHT TO EXCLUDE" SHOULD NOT BE CONFUSED WITH THE "RIGHT TO DO." IN OTHER WORDS, A PATENT DOES NOT CONVEY TO THE PATENTEE ANY RIGHTS TO DO THOSE THINGS. THE PATENT OWNER'S RIGHTS TO MAKE, USE, AND SELL THE INVENTION IS SUBJECT TO LAWS OTHER THAN THE PATENT LAW.

WITH RESPECT TO THE VOLATILE ANIMAL-PATENTING SITUATION, AND THE SHADOW OF UNCERTAINTY CAST UPON THE POTENTIAL PATENT RIGHTS OF THOSE OF YOU WHO MAY BE INVOLVED IN THIS CRITICALLY IMPORTANT FIELD OF RESEARCH, I AM CONFIDENT THAT THE PTO'S POSITION IS SOUND. THE BEST BET FOR ALL OF US (AT THE PTO AND MEMBERS OF THE IBA) IS TO CONTINUE OUR EFFORT TO BRING THE ETHICS DEBATE INTO PROPER FOCUS — AND TO HOPE THAT REASON PREVAILS.

(AS AN ASIDE, IT DOES SEEM QUITE IRONIC. EVER SINCE THE FOUNDING FATHERS CRAFTED ARTICLE I, SECTION 8 TO ENCOURAGE PROGRESS OF SCIENCE AND USEFUL ARTS, WE HAVE HOPED THAT INVENTORS WOULD COME UP WITH A "BETTER MOUSETRAP" — NOW, INSTEAD, THEY MAY BE COMING UP WITH A "BETTER MOUSE!")

ANOTHER PTO TOPIC OF VERY SPECIAL INTEREST TO MANY OF YOU WOULD BE THE REQUIREMENT FOR "DEPOSITS" OF BIOLOGICAL MATERIAL. DEPOSITS MAY BE NECESSARY TO SATISFY THE REQUIREMENTS OF THE PATENT LAW CONCERNING FULL DISCLOSURE OF THE INVENTION. (WE ALSO UNDERSCORED "DISCLOSURE," YOU MAY RECALL.)

THE IDEA IS THAT ONCE THE PATENT OWNER'S LIMITED EXCLUSIVE RIGHT TO THE INVENTION HAS EXPIRED, THE PUBLIC WILL BENEFIT FROM ITS

UNRESTRICTED USE. IT IS NOW RECOGNIZED, HOWEVER, THAT IN SOME INSTANCES A NEW BIOLOGICAL MATERIAL MAY NOT BE REPRODUCIBLE BY THE PUBLIC — EVEN WHEN DETAILED PROCEDURES AND A COMPLETE TAXONOMIC DESCRIPTION ARE INCLUDED IN THE PATENT SPECIFICATION.

AN "ARCHIVED" SAMPLE OF THE NEW MATERIAL MAY BE THE ONLY WAY WE CAN BE SURE THAT THE PUBLIC WILL EVER HAVE FULL ACCESS TO THE INVENTION. SATISFYING THIS REQUIREMENT WILL NOT BE EASY — THERE ARE A PLETHORA OF DETAILS TO CONSIDER AND MANY QUESTIONS MUST STILL BE ANSWERED.

THE PTO, JUST LAST MONTH, PUBLISHED AN ADVANCED NOTICE OF PROPOSED RULES WHICH ARE DIRECTED TOWARD ANSWERING THE "WHAT, WHERE, HOW, AND BY WHOM" OF THE DEPOSIT ISSUE. FOR THOSE WHO HAVE AN INTEREST IN THIS AREA, I HAVE BROUGHT COPIES OF THE ADVANCE NOTICE. (YOU MAY PICK UP A COPY AT THE END OF THIS SESSION.) WE WOULD WELCOME YOUR COMMENTS AND SUGGESTIONS.

MEANWHILE, WE ARE MOVING FORWARD IN A NUMBER OF OTHER AREAS TO UPGRADE THE OPERATION OF THE PTO, AND TO IMPROVE THE TIMELINESS AND QUALITY OF OUR SERVICE. I KNOW THESE ARE CONCERNS YOU SHARE.

RISING BACKLOGS HAVE BEEN OUR BIGGEST CHALLENGE. OVERALL, WE HAVE MADE HEADWAY IN REDUCING THE AVERAGE WAITING TIME FOR A PATENT GRANT. OUR TARGET IS 18 MONTHS. HOWEVER, THE INCREASING WORKLOAD IN THE BIOTECHNOLOGY AREA HAS BEEN STAGGERING. THE EXAMINING DIVISION HANDLING THE BULK OF THE BIOTECHNOLOGY APPLICATION FILINGS (ALONG WITH SOME OTHER TECHNOLOGIES) HAS SEEN ITS BACKLOG INCREASE FROM AROUND 3,900 PENDING APPLICATIONS ONLY TWO YEARS AGO, TO MORE THAN 7,800

TODAY. THE SITUATION HAS BEEN EXACERBATED BY OUR DIFFICULTY IN RECRUITING AND RETAINING NEW EXAMINERS. (YOU HAVE GIVEN US VERY TOUGH COMPETITION IN THAT AREA.)

OUR IMMEDIATE PLANS INCLUDE A REORGANIZATION TO CREATE A NEW EXAMINING DIVISION, OR GROUP, DEDICATED TO HANDLING ONLY BIOTECHNOLOGY PATENT APPLICATIONS. WE ARE RECRUITING THROUGHOUT THE COUNTRY FOR COLLEGE GRADUATES WITH APPROPRIATE BACKGROUNDS TO HANDLE THIS NEW FIELD, AND I HAVE GIVEN THE GO-AHEAD FOR BIOTECH SUPERVISORS TO HIRE AS MANY NEW EXAMINERS AS THEY CAN POSSIBLY ABSORB.

I HAVE ALSO ASKED THE OFFICE OF PERSONNEL MANAGEMENT TO GRANT "DIRECT HIRING AUTHORITY" TO THE PTO. THIS AUTHORITY, WHICH I AM OPTIMISTIC WE WILL RECEIVE, WILL CUT THE TIME-CONSUMING RED TAPE WE FACE IN SELECTING MICROBIOLOGISTS FROM THE CIVIL SERVICE REGISTER. YES! GOVERNMENT RED TAPE!

I SHOULD REMIND YOU THAT UNDER CERTAIN CIRCUMSTANCES THERE ARE PROVISIONS FOR HAVING AN APPLICATION EXAMINED OUT OF TURN. FOR EXAMPLE, IF THE INVENTION RELATES TO SAFETY OF RESEARCH IN THE FIELD OF RECOMBINANT DNA, APPLICANT MAY FILE A REQUEST THAT THE APPLICATION BE ADVANCED FOR EARLIER CONSIDERATION. OTHER "SPECIAL" CATEGORIES FOR SPEEDING UP APPLICATION PROCESSING INCLUDE:

-- THE SITUATION IN WHICH AN APPLICANT STATES THAT THE CLAIMED INVENTION IS ACTUALLY BEING INFRINGED;

-- OR WHERE APPLICANT IS READY TO MANUFACTURE OR COMMERCIALIZE THE INVENTION BUT NEEDS THE PATENT GRANT TO RAISE CAPITAL;

— OR WHERE APPLICANTS THEMSELVES PRESENT A THOROUGH PRE-EXAMINATION SEARCH AND THEY AGREE TO CERTAIN OTHER RESTRICTIONS TO HELP ACCELERATE THE PROCESS.

GRANTING SPECIAL STATUS DOES NOT IN ANY WAY CURE THE MASSIVE BACKLOG BUT IT DOES PREVENT A TOTAL ROADBLOCK IN EXCEPTIONAL CASES.

PENDENCY REDUCTION IS A VERY SERIOUS CHALLENGE, BUT I BELIEVE THAT AN EVEN MORE IMPORTANT CHALLENGE FOR THE PTO IS THE MAINTENANCE OF A HIGH QUALITY EXAMINATION SYSTEM. A PATENT GRANT OF LESS THAN ACCEPTABLE QUALITY IS WORSE THAN WORTHLESS -- IT IS LIKE A TIME-BOMB IN THE HANDS OF UNSUSPECTING PATENT OWNERS.

SO WE HAVE WORKED VERY HARD ON PATENT QUALITY. IT IS MY NUMBER ONE PRIORITY! EVEN IN OUR RECRUITING CAMPAIGN TO EXPAND THE PATENT EXAMINING CORPS, WE ARE HIRING THE BEST AND BRIGHTEST PEOPLE WE CAN FIND. IN THE PAST 6 YEARS, WE HAVE HIRED 1,100 EXAMINERS, AND THREE-FOURTHS OF THOSE HAVE BEEN HONORS GRADUATES.

IN ADDITION TO A QUALITY REVIEW PROGRAM THAT REVIEWS SAMPLES OF PATENT APPLICATIONS READY FOR PATENT GRANT, WE JUST STARTED A NEW OFFICE-WIDE PROGRAM TO REINFORCE QUALITY SERVICE IN ALL RESPECTS.

NOT ONLY ARE WE BRINGING IN THE BEST PEOPLE, BUT WE ARE GIVING THEM BETTER TOOLS TO WORK WITH, AS WELL. WE RECOGNIZE THAT ANY DECISION ON PATENTABILITY IS ONLY AS GOOD, OR AS VALID, AS THE INFORMATION IT IS BASED UPON. WE HAVE SPENT MILLIONS TO MODERNIZE OUR LITERATURE SEARCH CAPABILITY SO THAT EXAMINERS CAN DETERMINE WHETHER THE CLAIMED INVENTIONS ARE NEW. OUR PLANS ARE TO CREATE AN AUTOMATED PATENT SYSTEM. THIS WILL BE AN ELECTRONIC REPLACEMENT FOR OUR MASSIVE

PAPER SEARCH FILE OF 28 MILLION DOCUMENTS. WE PLAN AN ON-LINE SEARCH SYSTEM WITH 100% INTEGRITY (NO LOST DOCUMENTS; NO MISSING INFORMATION). BUT, EVEN WITH ALL THAT EFFORT AND EXPENDITURE, WE KNOW IT WON'T BE ENOUGH FOR COPING WITH THE SPECIAL CHALLENGES WE FACE PROCESSING BIOTECHNOLOGY PATENT APPLICATIONS.

WE HAVE MORE THAN 1,800 APPLICATIONS PENDING WITH DNA, RNA, AND PROTEIN SEQUENCES THAT MUST BE THOROUGHLY SEARCHED. THOSE OF YOU WHO ARE FAMILIAR WITH THE SPECIAL ELECTRONIC DATABASES BIONET, GENBANK, AND OTHERS, KNOW JUST HOW IMPORTANT SEQUENCE SEARCHING CAN BE — AND HOW COSTLY, AS WELL. WE PLAN TO COMMIT FISCAL '88 FUNDING TO GIVE BETTER ACCESS TO THOSE SPECIAL SEQUENCE DATABASES, AND TO HELP US USE THEM MORE EFFECTIVELY AND EFFICIENTLY. OUR PLAN IS TO ACQUIRE NEW HARDWARE AND TO PURCHASE THE NECESSARY SOFTWARE TO BRING THIS CAPABILITY IN-HOUSE.

ALSO, I WANT TO NOTE THAT WE ARE LOOKING TO YOU FOLKS FOR SOME HELP IN STANDARDIZING THE SEQUENCE FORMATS, AND IN CONVINCING THE GENBANK FOLKS OVER AT N.I.H. TO CONSIDER INCLUDING PATENT LITERATURE IN THEIR DATABASE.

FINALLY, LET ME TELL YOU ABOUT OUR PLANS AND PRIORITIES ON THE INTERNATIONAL FRONT. SINCE A UNITED STATES PATENT ONLY AFFORDS PROTECTION WITHIN THE UNITED STATES, IT'S NECESSARY TO USE THE RESPECTIVE PATENT SYSTEMS OF OTHER COUNTRIES TO GAIN GLOBAL EXPLOITATION OF A NEW INVENTION. UNFORTUNATELY, AS YOU MAY HAVE FOUND, THAT IS NOT A SIMPLE THING TO DO.

THE PROCESS OF APPLYING FOR A PATENT AND THE TECHNICALITIES OF ENFORCING THAT PATENT IN THE VARIOUS COUNTRIES AROUND THE WORLD CAN BE AS DIVERSE AS THE CULTURES OF THOSE COUNTRIES.

THROUGHOUT THE WORLD, ABUSES OF AN INVENTOR'S RIGHTS CAN BE AS BLATANT AS OPEN PIRACY OR AS SUBTLE AS PROCEDURAL RED TAPE. AT BEST, DIFFERENCES IN PATENT SYSTEMS AMONG OUR TRADING PARTNERS CAUSE CONFUSION, ADDED EXPENSES, AND COSTLY TIME-DELAYS. WE'RE TALKING ABOUT LOSS OF MARKETS OVERSEAS ... AND LOSS OF JOBS HERE AT HOME.

LACK OF CONSISTENCY, OR CONFORMITY, OR STANDARDIZATION, OR HARMONIZATION — WHATEVER YOU WANT TO CALL IT — BOILS DOWN TO MORE THAN JUST A HEADACHE FOR A PATENT OWNER. IT IS A BARRIER TO WHAT SHOULD BE A FREE-FLOWING INTELLECTUAL PROCESS.

THAT'S WHY WE SEE HARMONIZATION AS SO IMPORTANT, AND THAT'S WHY THE UNITED STATES GOVERNMENT HAS BEEN PUSHING SO HARD FOR IT THROUGHOUT THE WORLD — IN BOTH MULTILATERAL AND BILATERAL DISCUSSIONS. THIS, PERHAPS, HAS MORE SIGNIFICANCE TO THE BIOTECHNOLOGY INDUSTRY THAN TO MOST. IT SEEMS THAT PATENT COVERAGE ON CHEMICALS, DRUGS, PROTEINS, ENZYMES, ANIMALS, AND SO ON, RANGES FROM <u>TOTAL CONFUSION</u> TO <u>SPECIFIC EXCLUSION</u> IN PATENT OFFICES AROUND THE GLOBE.

OUR FOCUS IN THIS HARMONIZATION EFFORT HAS BEEN AS NARROW AS THE SUCCESSFUL BILATERAL TALKS WITH SOUTH KOREA, AND AS BROAD AS THE GLOBAL EFFORT IN THE WORLD INTELLECTUAL PROPERTY ORGANIZATION.

I AM ESPECIALLY PLEASED TO SEE PROGRESS IN OUR ON-GOING TRILATERAL TALKS WITH THE JAPANESE AND EUROPEAN PATENT OFFICES. ONE OF OUR MAJOR HARMONIZATION PROJECTS WITHIN THAT FORUM IS A COMPARATIVE STUDY OF OUR RESPECTIVE PATENT PRACTICES INVOLVING BIOTECHNOLOGY

INVENTIONS.[8] THIS STUDY TO REVEAL OUR DIFFERENCES IS THE NECESSARY FIRST STEP TOWARD ELIMINATING OUR DIFFERENCES.

SUCCESS IN THIS AREA AS IN ALL OTHER HARMONIZATION AREAS WILL DEPEND UPON TWO MAJOR INGREDIENTS: A GRAND SPIRIT OF COOPERATION AND A WILLINGNESS TO COMPROMISE.

IN CONCLUSION, I WOULD SAY THAT THE PTO RECOGNIZES ITS RESPONSIBILITIES IN MEETING THE CHALLENGE PUT BEFORE IT BY EXPLODING, "SUNRISE" TECHNOLOGIES. WE KNOW THAT IF WE ARE TO KEEP PACE WITH THE INNOVATION, WE ALSO HAVE TO BE INNOVATIVE.

THANK YOU.

LEGAL AND REGULATORY ISSUES
AFFECTING BIOTECHNOLOGY

Shearson Lehman Brothers

NEW YORK CITY - September 30, 1987

The Basics of Patents

Charles E. Van Horn, Director
Organic Chemistry and Biotechnology
U.S. Patent and Trademark Office

I. Patent System

II. Patent Grant

A. Rights - Every patent shall...grant to the patentee...the right to exclude others from making, using, or selling the invention throughout the United States...

B. Term

1. 17 years from date patent is granted

2. Extension of up to five years in limited circumstances where human drug product, medical device, food or color additive has undergone premarketing approval at the Food and Drug Administration

3. No publication until patent is granted

C. Specification - written description of the invention

1. Directed to a person skilled in the art to which the invention pertains

2. How to make and use the invention

3. Best mode contemplated by the inventor of carrying out the invention

4. Deposits of biological material

D. Claim

1. Defines subject matter which the applicant regards as the invention

2. Product, process of making, process of using, machine

III. Requirements for Patentability

A. Statutory subject matter - 35 USC 101

B. Utility - 35 USC 101

C. Novelty - 35 USC 102

1. Grace period

2. Loss of right to a patent

3. Access by public

D. Non-obviousness - 35 USC 103

1. Scope and content of prior art

2. Differences between claims and prior art

3. Level of skill in the art

4. Secondary considerations such as unexpected results, long-felt need, commercial success

IV. PTO Application Processing

A. Organization

1. 15 examining groups (4 chemical, 6 electrical, 5 mechanical)

2. 1440 examiners (1330 on 10-1-86)

B. Examination process - goal is to examine and dispose of an average patent application 18 months after filing by end of fiscal year 1989

C. Office/Group 120 Filings

1. Office - 121,500 applications filed in FY 86
126,000 applications filed (est.) in FY 87

2. Group 120 - 12,000 applications filed in FY 86
12,450 applications filed (est.) in FY 87

3. Group 120 (Biotech) Status

V. Other PTO Proceedings

A. Interference - determine the first inventor

B. Reissue Patent - filed by patent owner to correct defects in original patent

C. Reexamination - a proceeding that may be initiated by anyone to determine the patentability of patented invention over prior art patents or printed publications

United States Patent [19]
Dorsett

[11] **Patent Number: 4,695,537**
[45] **Date of Patent: Sep. 22, 1987**

[54] **PARTICLES SENSITIZED WITH DETERGENT-TREATED ANTIGEN FOR AGGLUTINATION IMMUNOASSAY**

[75] Inventor: **Preston H. Dorsett, Memphis, Tenn.**

[73] Assignee: **The University of Tennessee Research Corp., Knoxville, Tenn.**

[21] Appl. No.: **727,661**

[22] Filed: **Apr. 25, 1985**

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 380,337, May 21, 1982, Pat. No. 4,590,156.

[51] Int. Cl.⁴ G01N 33/546; G01N 33/547
[52] U.S. Cl. 435/5; 435/7; 435/810; 436/310; 436/532; 436/533; 436/534; 436/808

[58] Field of Search 436/533, 534, 825, 510, 436/532, 808; 435/5, 7, 810

[56] **References Cited**

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4,311,788	1/1982	Hesch	436/825 X
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Primary Examiner—Sidney Marantz
Attorney, Agent, or Firm—Elliot M. Olstein

[57] **ABSTRACT**

An agglutination immunoassay for antibody wherein antigen for sensitizing a solid particulate support is treated with detergent. The resultant antigen-sensitized support is resistant to self-agglutination.

28 Claims, No Drawings

PARTICLES SENSITIZED WITH DETERGENT-TREATED ANTIGEN FOR AGGLUTINATION IMMUNOASSAY

This application is a continuation-in-part of U.S. Application Ser. No. 380,537, filed on May 21, 1982 U.S. Pat. No. 4,590,156.

This invention relates to antigens, and more particularly to the use of antigens for the production of sensitized solids, and the use of antigen sensitized solids for testing for antibodies. Most particularly, the invention relates to viral antigens supported on a particulate support and the use thereof in an assay.

U.S. Pat. No. 4,195,074 discloses a process for producing soluble rubella virus antigen, and the use thereof in an agglutination test for rubella virus antibody. In accordance with U.S. Pat. No. 4,195,074, the cell culture fluid from rubella virus-infected cells is subjected to immunosorbent separation through a column containing IgG derived from human serum known to contain antibodies reactive with rubella virus antigen followed by elution of the rubella virus antigen material from the column and selection of the soluble antigen by gel permeation chromatography. The antigen may then be employed for sensitizing erythrocytes, and the sensitized erythrocytes are used to determine antibody in human serum samples by direct agglutination.

In accordance with one aspect of the present invention, there is provided a solid support sensitized with an antigen with the antigen preferably being derived from an intracellular parasite, in particular, a virus.

More particularly, the antigen, which is supported on the solid particle(s) (a particulate support) has been treated with a detergent or surfactant so as to produce a particulate support sensitized with antigen which is more resistant to self-agglutination. Although applicant does not intend to be bound by any reasoning, it is believed that treating the antigen with the surfactant disrupts the antigen on the solid particles and such disrupted antigen on solid particles results in an increase in the resistance to self-agglutination. It is believed that the treatment disrupts the antigen and that such disruption may reduce the molecular weight which improves resistance to self-agglutination.

In accordance with a preferred embodiment, the antigen is treated with the detergent prior to being supported on the solid support; however, it is also possible to treat the antigen after being supported. Treatment on the support generally results in a loss in titer and, therefore, is not preferred.

The antigens which are treated prior to being supported on the particulate support are antigens which have a high molecular weight in excess of 500,000 daltons and in particular, antigens from an intra-cellular parasite such as a virus, toxoplasma, chlamydia or mycoplasma.

The treatment of the antigen with the detergent prior to being supported on the particulate support, may occur simultaneously with recovery of the antigen and prior to being supported on the solid particle(s).

Thus, for example, a viral antigen may be recovered from intact virus by treating the virus with a detergent (surfactant) which disrupts the virus to provide the viral antigen and in such a case, the viral antigen may be supported on a solid particle to produce a sensitized particle which resists self-agglutination in that the viral antigen is treated with the detergent or surfactant prior to being supported on the solid support.

In the case where the antigen is recovered by a procedure which does not involve the use of a detergent or surfactant, then the recovered antigen is separately treated to disrupt the antigen prior to supporting the antigen on the solid particles so as to provide sensitized particles which resist self-agglutination.

The surfactant or detergent which is used for treating the antigen may be any one of a wide variety of surfactants or detergents which disrupt the antigen, without destroying the antigenic characteristics, including cationic, anionic and non-ionic surfactants. Such surfactants are well known in the art, and as representative examples, there may be mentioned alkali metal salts of sulfates, soaps, sulfated or sulfonated oils, various amines, quaternary salts, condensation products with ethylene oxide, etc. Preferred detergents for such use are alkali (lithium or sodium) dodecyl sulfate, sulfobetain, deoxylcholate and laurolylsarcosine (Sarcosyl).

As hereinabove indicated, it is believed that the antigen is disrupted so as to reduce its molecular weight and the detergent is preferably employed in an amount and for a time such as to effect such molecular weight reduction. In accordance with a preferred embodiment, the molecular weight of the antigen does not exceed 200,000 daltons and most generally does not exceed 150,000 daltons, as determined by sucrose gradient centrifugation or exclusion chromatography.

In general, the surfactant or detergent is employed in a weight ratio of surfactant to antigen of from about 0.05 to 1 to about 5 to 1. The selection of an optimum amount is deemed to be within the scope of those skilled in the art from the teachings herein.

After treating the antigen with the surfactant or detergent, the antigen may be supported on a solid particulate support. The support may be any one of a wide variety of supports, and as representative examples of suitable supports there may be mentioned synthetic polymer supports, such as polystyrene, polypropylene, substituted polystyrene (e.g., aminated or carboxylated polystyrene), polyacrylamides, polyamides, polyvinylchloride, etc.; glass beads, agarose; cellulose; etc. The supports may be provided with reactive groups; e.g., carboxyl groups, amino groups, etc. to permit direct linking of the virus antigen to the support.

The antigen may be supported on the support by a variety of techniques including adsorption; covalent coupling; for example, by activation of the support, or by the use of a suitable coupling agent or by the use of reactive groups on the support. Such procedures are generally known in the art, and no further details are deemed necessary for a complete understanding of the present invention.

In accordance with a particularly preferred embodiment, the antigen is supported on a particulate support by an adsorption technique, although other techniques may be used.

In accordance with preferred embodiment, the particulate support is either a polystyrene, aminated polystyrene, carboxylated polystyrene or a polyvinylchloride, although, it is to be understood that the scope of the invention is not limited to such supports.

As hereinabove indicated, the antigen may be supported on the support by the use of an adsorption technique, or by covalent coupling with a coupling agent. As representative examples of suitable coupling agents there may be mentioned: dialdehydes; for example, glutaraldehyde, succinaldehyde, malonaldehyde, etc.;

unsaturated aldehyde, e.g., acrolein, methacrolein, crotonaldehyde, etc.; carbodiimides; diisocyanates; dimethyladipimate; cyanuric chloride, etc. The selection of a suitable coupling agent should be apparent to those skilled in the art from the teachings herein.

Similarly, the antigen may be supported by activation of a suitable support; for example, cyanogen bromide activated agarose.

The antigen which is treated and supported on a particulate support in accordance with the present invention is preferably a viral antigen. The viral antigen may be recovered in accordance with a variety of procedures.

In accordance with one procedure, which is particularly applicable to recovering a soluble rubella virus antigen, a whole virus is treated with a surfactant or detergent which disrupts the virus to provide the virus antigen, in particular, rubella virus antigen, without destroying the antigenic characteristics thereof. The surfactant or detergent is of the type hereinabove described. In such a procedure, it is not necessary to employ a separate step for treating the viral antigen in addition to the step for recovering the viral antigen by use of the detergent or surfactant.

The surfactant is employed in an amount which is sufficient to disrupt and solubilize the virus and which does not destroy the antigenic characteristics thereof (too much detergent may destroy the antigenic characteristics). In general, the surfactant to virus weight ratio is an amount of from 0.2:1 to about 5:1, preferably from about 0.5:1 to 1:1. The selection of an optimum amount is deemed to be within the scope of those skilled in the art from the teachings herein.

The treatment of the purified virus is effected at a temperature which does not denature the virus proteins, with such temperature generally not exceeding about 30° C., with a temperature of from 20° C. to 25° C. being most convenient. Similarly, the pH is selected so as to maintain stability, with the pH being generally at 8.5, with the optimum pH generally being in the order of from 8.0 to about 9.0.

The treatment of the purified virus with the surfactant is for a period of time sufficient to disrupt the virus and effect solubilization thereof. In general, such disruption and solubilization can be accomplished in time periods in the order of from 5 to 120 minutes, however, in some cases longer or shorter times may be applicable.

The selection of an optimum treatment time is deemed to be within the scope of those skilled in the art from the teachings herein.

Applicant has found that by using a surfactant to disrupt and solubilize the whole rubella virus, as hereinabove described, it is possible to provide soluble rubella virus antigen which retains its antigenicity.

A procedure for disruption and solubilization of whole virus, as hereinabove described, has been previously practiced in the art; for example, Vaheri et al. "Structural Proteins and Subunits of Rubella Virus", *Journal of Virology*, P. 10–16 (Jan. 1972). In addition, it is known that such a procedure is capable of recovering the structural proteins of the whole rubella virus, with there being three principal structural proteins, namely a structural protein with a molecular weight in the order of from 60,000 to 65,000 daltons, a structural protein with a molecular weight in the order of from 40,000 to 50,000 daltons, and a structural protein having a molecular weight in the order of from 32,000 to 38,000 daltons. Applicant has also found evidence of structural proteins having molecular weights of from 100,000 to 120,000 daltons.

Applicant has found that the structural proteins recovered by such a procedure retain antigenic characteristics, and in addition, such structural proteins can be used in an assay for rubella antibody. Furthermore, applicant has found that such structural proteins are capable of detecting early phase rubella antibody, i.e., the rubella antibody present in serum or plasma within ten days of onset of rubella rash. The term "rubella virus antigen" as used herein encompasses one or more of such structural proteins recovered by such procedure.

The hereinabove described technique for disruption and solubilization of whole rubella virus to provide soluble rubella virus antigen is also applicable to providing virus antigen from other viruses; e.g., those hereinafter disclosed with reference to a purification of virus. Such viral antigens may then be supported on a solid support to provide a solid sensitized with the viral antigen for use in an assay.

In accordance with an aspect of the present invention, applicant has found that disruption and solubilization of whole rubella virus produces a soluble product which is antigenic and which is capable of reacting with rubella antibody, including the early phase antibody. Thus, by using a product prepared by such a procedure in an assay for rubella antibody; and in particular, on a solid support, it is possible to detect rubella antibody even during the early phase.

The recovered product is of particular value for a direct agglutination assay, and applicant has found that such soluble rubella virus antigen may be supported on a latex particle (in particular, a polystyrene) without the problem of self-agglutination.

The purified whole virus which is treated with surfactants is a virus which is produced in a tissue culture by procedures known in the art, and which is subsequently purified to remove non-virus lipids, nucleic acids, and non-viral proteins.

The tissue culture growth of rubella virus wherein rubella virus infected cells are raised in a suitable culture medium is well known in the art. The cells that are suitable for tissue culture growth to propagate the rubella virus include Vero cells, Baby Hamster Kidney, Procine Stabile Kidney; Serum Institute Rabbit Cornea and the like. In general, tissue cultures conventionally used for producing rubella virus are also suitable for the purposes of the present invention.

The virus may then be purified by procedures known in the art; e.g., as disclosed by Vaheri, et al., supra. In accordance with a preferred embodiment, the virus is purified in accordance with a new procedure.

More particularly, such procedure for purifying virus involves treating concentrated virus with hydroxylapatite gel in an aqueous solution of controlled ionic strength and pH.

More particularly, after filtration and concentration, the virus is contacted with hydroxyl apatite gel in an aqueous solution having an ionic strength which is great enough to minimize or prevent adsorption of the virus by the gel, and which is low enough to allow the non-virus proteins to be adsorbed by the gel. The ionic strength is maintained by use of phosphate ions, with the phosphate ions being present at a molarity of from 0.05M to 1.5M to provide for effective adsorption of non-virus proteins and nucleic acids, without significant

adsorption of the virus. The phosphate molarity in most cases is at least 0.08M.

In addition, the adsorption is conducted at a pH in the order of from 6 to 9, most generally in the order of from 7 to 8. The pH of the solution is maintained by the use of a suitable buffer. The adsorption may be conducted in the presence of EDTA at a concentration from 0.01M to 0.001M. EDTA, as well as other chelating agents, increases adsorption of non-viral proteins and nucleic acids, and aids in minimizing the adsorption of viral proteins.

By proceeding in accordance with such purification, the high molecular weight proteins and nucleic acids are adsorbed by the gel to thereby separate the virus protein from the non-viral proteins having similar molecular weights.

After such adsorption, the lower molecular weight proteins still remaining in the fluid may be separated by conventional procedures. Thus, for example, further separation may be accomplished by centrifugation through a barrier layer or cushion as known in the art. In particular, the virus protein is centrifuged through a suitable barrier layer such as sucrose, glycerol, cesium chloride, cesium sulfate and the like, with the lower molecular weight proteins remaining above the barrier, and the virus being centrifuged through the barrier, as a separate layer. The fluid containing the low molecular weight proteins and the barrier layer are then removed leaving a virus protein essentially free of non-virus proteins, nucleic acids, lipids, and the like. In general, the purified virus contains less than 1%, most generally less than 0.1% of non-virus lipids, nucleic acids and proteins

Such purified virus may then be treated with a surfactant to disrupt the virus and effect solubilization thereof to thereby provide a virus antigen, as hereinabove described.

It is to be understood that, although the hereinabove described procedure for purifying the rubella virus is preferred, other procedures for separating non-virus proteins, lipids and nucleic acids can also be employed for purifying the rubella virus for subsequent treatment with surfactant to thereby produce the soluble rubella virus.

The antigen and in particular, a viral antigen, may be obtained by other procedures. Thus, for example, as described in U.S. application Ser. No. 700,806, filed on Feb. 11, 1985, antigen may be recovered from cells containing an intra-cellular parasite (in particular, a virus) by extracting the antigen from the cells with an aqueous salt solution.

More particularly, the aqueous salt solution is hypertonic with respect to the osmolarity of the cells and is a salt solution which does not adversely affect the immunoreactivity of the extracted antigen. The aqueous salt solution is one which extracts the antigen from the cell without essential destruction of the cells; i.e., the cells remain essentially intact.

The salt may be either an inorganic or an organic salt which is soluble in water, and as representative examples of such salts, there may be mentioned: potassium chloride, guanidine hydrochloride, magnesium chloride, potassium thiocyanate, sodium chloride, etc. Potassium chloride, magnesium chloride and guanidine hydrochloride are particularly preferred in that the use of such salts results in a higher yield of antigen.

The concentration of salt in the solution is one which provides a hypertonic solution and which effectively extracts the antigen from the cells. In general, the salt concentration is in the order of at least 1.0M and no greater than 5.0M, and preferably at least 2.0M and no greater than 3.5M.

The extraction is accomplished at temperatures which will not denature the antigen. The temperature generally does not exceed about 30° C. The pH of the salt solution is generally maintained at a value so as to maintain stability, with the pH generally being from pH 6 to pH 10. A suitable buffer may be used to maintain the pH.

The cells may be contacted with the salt solution by any one of a wide variety of procedures. Such contacting may be readily accomplished by placing the infected cells in the salt solution and stirring; e.g., with a magnetic stirrer.

After the cells have been contacted for a period of time sufficient to extract the antigen from the cells, the cells are removed from the salt solution; for example, by centrifugation.

The remaining supernatant contains the antigen, and the antigen may be stored for use at a subsequent time, or may be used as hereinafter described.

The salt may be removed from the supernatant, for example, by dialysis of the supernasant against a suitable buffer.

The above procedure is particularly applicable to extracting viral antigen from cells infected with a virus and most particularly to recovering CMV antigen from CMV infected cells. The cells which are infected with CMV are preferably primary human foreskin cells; however, it is to be understood that other cells may be used within the spirit and scope of the invention; for example, human diploid cells other than foreskin cells.

The viral antigens recovered by this procedure and in particular, CMV antigen, after treatment with detergent, may be supported on a solid particulate support for use in an assay.

An antigen sensitized particulate support prepared in accordance with the invention is preferably prepared for use in an assay in which antibody is determined by an agglutination technique. The particulate support is provided with an effective amount of the antigen for the assay, while preventing excessive amounts which may result in bridging of the antibody to a single particle. In general, the weight ratio of antigen to support is from 1:100 to 1:5000. The selection of an optimum amount is deemed to be within the scope of those skilled in the art from the teachings herein.

In accordance with one technique, after the antigen is adsorbed on the particles, the support, including the adsorbed antigen, is further coated with protein which does not adversely affect the subsequent immunochemical reaction in order to provide a protein coating on the portion of the support which does not include the antigen. As should be apparent, the protein coating should not immunologically react with either the antigen or with sera to be used in the assay. As examples of suitable proteins there may be mentioned: bovine serum albumin, ovalbumin, and the like. The selection of a suitable protein to saturate the spaces between the antigen on the support is deemed to be within the scope of those skilled in the art from the teachings herein.

It is to be understood that such coating with protein is not required for producing sensitized particles for use in an agglutination assay.

After the antigen has been supported on a solid support, as generally practiced in the art for the production of sensitized particles for use in an agglutination assay,

the sensitized particles are treated with a liquid containing polyoxyethylene sorbitan monolaurate (Tween 20) at a weight ratio to the polystyrene of 0.05:1 to 10:1.

The sensitized particles are preferably a synthetic polymer and in particular, a polystyrene [substituted (carboxylated or aminated) or unsubstituted] or polyvinylchloride latex. Applicant has found that sensitization of such particles with antigen prepared, as hereinabove described, produces a sensitized particle which is more resistant to self-agglutination, whereby such sensitized latex particles may be effectively employed in a direct agglutination assay for antibody. In the case where the antigen is rubella virus antigen, such sensitized particles are capable of detecting early phase rubella antibody. In addition, such sensitized particles are capable of providing a direct agglutination assay having a high sensitivity for rubella antibody.

The antigen sensitized particles prepared in accordance with the invention are suitable for use in a kit and assay for antibody by a direct agglutination procedure. Such kit may include, in addition to the sensitized particles, as hereinabove described, in a suitable container therefor, a reactive serum control (contains antibody) and a non-reactive serum control (no antibody) in suitable containers therefor. In accordance with a preferred embodiment, in addition to the reagents, there is provided a test card on which the assay is effected. The test card has a flat testing surface which includes suitably marked areas (for example, a test circle) for placing one or more samples to be assayed, as well as suitably marked areas for each of the serum controls. The test card and reagents may be included in a single kit package.

In the agglutination assay, undiluted serum or diluted serum (e.g., 1:10) is contacted with the sensitized particles followed by mixing, with the presence of the antibody against the antigen (in particular, a viral antigen) being evidenced by visible agglutination.

Such antigen sensitized particles may also be employed in a quantitative assay for antibody; in particular, rubella virus antibody and CMV antibody.

In a quantititative assay, the sample to be assayed is serially diluted, as appropriate, and to each serial dilution there is added the particles sensitized with the antigen. The quantity of antibody in the sample is determined from the highest dilution giving any agglutination of the sensitized particles.

The quantitative or qualitative assay for antibody may be effected on a card surface wherein the surface includes suitably marked areas for placing the sample and control to which the sensitized particles are added.

The invention has particular applicability to sensitizing particles for use in determining rubella virus or cytomegalo virus (CMV); however, the scope of the invention is not limited to such viruses.

The invention will be further described with respect to the following examples: however, the scope of the invention is not to be limited thereby:

EXAMPLE I

Production and Purification of Rubella Virus.

Confluent roller cultures (680 cm^2) of Vero cells (a continuous culture line of cells derived from African Green monkey kidney) were innoculated with approximately 0.01 PFU of rubella virus per cell and maintained in a standard culture medium (Medium 199) containing 0.025 herpes buffer, pH 7.4, and 2% (vol/vol) of the filtrate obtained by forcing fetal bovine serum through a xembrane designed to retain molecules of 100,000 molecular weight and greater (Amicon XM-100 membrane). The medium was changed daily, and the culture fluids having a hemagglutination titer greater than 16 were made to contain 0.01M Tris base and 0.01M EDTA. After incubation at 4° C. for 1 hour, they were concentrated in an Amicon hollow fiber dialyzer-concentrator to 1/10 the original volume. After clarification at 5,000×g for 20 minutes, the pH was adjusted to 7.6 at 22° C. and 1/10 volume of hydroxylapatite suspension was added, and the slurry was incubated at 4° C. with mixing, overnight. The hydroxylapatite was removed by centrifugation at 5,000×g for 15 minutes, after which 30 ml of the concentrate was layered over 9 ml of 69% (wt/wt) glycerol in a Beckman SW28 tube The virus was sedimented at 82,000×g for 16 hours at 4° C., and the resultant pellet was resuspended in 0.01M carbonate buffer, pH 9.5 (coating buffer) The purified virus was assayed for hemagglutinin content and stored at -70° C.

EXAMPLE II

Solubilization of Purified Virus.

The purified virus in 0.01M carbonate buffer, pH 9.5, was solubilized by treatment with sodium dodecyl sulfate (SDS). The purified virus was made to contain 0.05% (w/v) SDS and was incubated for 30 minutes at room temperature.

EXAMPLE III

Preparation of Sensitized Latex.

Commercial suspensions of polystyrene latex (0.9 micron diameter particles) were washed four times with 25 volumes each of the coating buffer and were resuspended in the coating buffer to provide 3% solids (w/-vol.). The latex suspension was added directly to the solubilized virus at a ratio of 2 volumes of the 3% latex to 1 volume of solubilized virus and the suspension was mixed by tumbling for 16 hours at room temperature. The sensitized latex was washed twice with 20 volumes of 1% bovine serum albumin in phosphate buffered saline (BSA-PBS) and resuspended at 0.5% in 1% BSA-PBS contained 0.05% polyoxyethylene sorbitan monolaurate surface active agent (Tween 20) and 0.02% gentamiacin.

EXAMPLE IV

Latex Agglutination Test for Rubella Virus Antibodies.

Glass plates with 1.4 cm fused circles were employed. Serial 2-fold dilutions of serum were prepared in 1% BSA-PBSTween 20 and 25 ul of each dilution was placed in separate wells. After adding 25 ul of sensitized latex, the serum and latex suspension was mixed and rotated 100 rpm for 5 minutes. The presence of antibody against rubella virus was evidenced by visible agglutination.

EXAMPLE V

Purified virus prepared in accordance with Example I was treated with a 1% aqueous solution of sarcosyl for 30 minutes at room temperature in coating buffer to disrupt and solubilize the virus.

The pH of the solubilized virus was adjusted to 6.5 with hydrochloric acid and mixed with two volumes of 3% carboxylated polystyrene latex (in phosphate buffer, pH 6.5) for 1 hour at 4° C.

To the solution was added 10 mg of a carbodiimide coupling agent and the mixture was mixed overnight at 4° C.

After centrifugation, the solids were resuspended in phosphate buffered saline (PBS) followed by centrifugation and resuspension in PBS containing 1% BSA and 0.05% Tween 20.

The procedure covalently bound the soluble rubella virus antigen to the latex.

EXAMPLE VI

In accordance with a preferred procedure, there is provided a test card for rubella antibody. The test card includes a marked circle for a reactive control, a marked circle for non-reactive control, as well as one or more test sample circles.

25 ul of undiluted serum sample is placed in appropriately marked sample circle, and 25 ul of the reactive and non-reactive controls are placed in their respective circles.

With a micropipettor, there is added sensitized latex of Example III (approximately 15 ul), followed by rotation on a rotator (about 8 minutes), and gentle hand rotation.

The card is read microscopically in the wet state under a high intensity incandescent lamp.

The reactive control should show definite agglutination and the non-reactive control should show no agglutination.

Any serum samples showing any agglutination should be reported as reactive.

EXAMPLE VII

Primary human foreskin cells are infected with AD 169 CMV and incubated for 7 to 10 days at 37° C., followed by harvesting of the infected cells. The cells are scraped into phosphate buffered saline (PBS), and the cells are collected by centrifugation followed by resuspending of the cells in 3M KCL in 0.1M glycine, NaOH .pH 7.5. The mixture is maintained at 4° C. for 24 hours, with gentle mixing, to extract CMV antigen from the infected cells. After such period, the cells are removed by centrifugation and the supernatant is dialyzed against 1000 volumes of 0.1M Glycine. NaOH pH 7.5. The CMV antigen may be stored by freezing at -70° C.

After determining the protein content from the optical density at 260 mm and 280 mm, the CMV antigen is treated with SDS (0.25 mg. SDS per mg. of CMB antigen).

Commercial suspensions of polystyrene latex (0.9 micron diameter particles) are washed with carbonate buffer and then resuspended in the carbonate buffer to provide 3% solids (volume to volume).

The hereinabove treated CMV antigen is added to the 3% latex suspension and incubated at 4° C. overnight with tumbling.

The latex is washed with phosphate buffered saline and then resuspended in a phosphate buffered saline solution to which has been added 1% (%/v) bovine serum albumin and 0.1% (%/v) polyoxyethylene sorbitan monolaurate surface active agent (Tween 20) and 0.02% gentamicin. The sensitized latex is allowed to cure for 24 hours at 4° C. with gentle stirring.

The sensitized latex may be employed in a test for CMV antibody by use of a test card which includes a marked circle for a reactive control, a marked circle for a non-reactive control, as well as one or more test samples circles.

25 ul of undiluted serum sample is placed in an appropriate marked serum sample circle, and 25 ul of the reactive and unreactive controls are placed in their respective circles.

With a micropipettor, there is added the sensitized latex (approximately 15 ul), prepared as hereinabove described, followed by rotation on a rotator, and gentle hand rotation.

The card is read microscopically in the wet state under a high intensity incandescent lamp while rotating gently by hand.

The reactive control should show definite agglutination and the non-reactive should show no agglutination. Any serum sample showing any agglutination should be reported as reactive.

Although the invention has been previously described with respect to CMV and rubella antigen, and an assay employing supported CMV and rubella antigen for determining CMV and rubella antibody, it is to be understood that the teachings are also applicable to other viral antigens, including but not limited to: other herpes viruses, such as varicella Zoster, Epstein-Barr (infectious Mono-Nucleosis); measles virus (rubeola); para-influenza viruses; influenza virus; dengue virus, etc.

Similarly, the invention is applicable to supporting on a particulate support antigens from intra-cellular parasites other than viruses, such as toxoplasma, chlamydia, microplasma, etc.

The above modifications and others should be apparent to those skilled in the art from the teachings herein.

The present invention is advantageous in that it is possible to support an antigen, in particular, CMV or rubella antigen, on a particulate support wherein the antigen sensitized particles are resistant to self-agglutination; in particular, where the antigen is supported on latex particles for use in an agglutination type of assay. These and other advantages should be apparent to those skilled in the art from the teachings herein.

Numerous modifications and variations of the present invention are possible in light of the above teachings and, therefore, within the scope of the appended claims, the invention may be practiced otherwise than as particularly described.

What is claimed is:

1. A composition, comprising:

a solid particulate support and a detergent-treated antigen supported on said support, said antigen being an intracellular parasite antigen, said antigen having been treated with a detergent to provide a solid support sensitized with the detergent-treated antigen which is is resistant to self-agglutination.

2. In a kit for determining antibody by an agglutination technique, the improvement comprising,

said kit including in a reagent container the solid particulate sensitized with the detergent-treated antigen of claim 1.

3. The kit of claim 2 wherein said kit further includes a test card having a flat surface for receiving assay samples.

4. The kit of claim 3 wherein the solid particulate support is polystyrene latex.

5. The kit of claim 3 and further comprising in separate reagent containers a reactive serum control antibody and a non-reactive serum control free of antibody.

6. The composition of claim 1 wherein said antigen has been treated with a detergent prior to being supported on the support.

7. In a direct agglutination assay for an antibody employing solid particles sensitized with antigen, the improvement comprising:

contacting a sample containing a suspected antibody with, the solid particles sensitized with the detergent-treated antigen of claim 2, said suspected antibody becoming immunobound by said detergent-treated antigen.

8. The assay of claim 7 wherein the antigen is a viral antigen.

9. The assay of claim 7 wherein the antigen is a rubella virus antigen.

10. The composition of claim 6 wherein the solid support is a synthetic polymer.

11. The composition of claim 10 wherein the synthetic polymer is selected from the group consisting of polyvinylchloride, polystyrene, aminated polystyrene and carboxylated polystyrene.

12. The composition of claim 10 wherein the antigen is covalently coupled to the solid support.

13. The composition of claim 10 wherein the antigen is adsorbed on the solid support.

14. The composition of claim 13 wherein the antigen is a herpes virus antigen.

15. The composition of claim 13 wherein the detergent is an alkali dodecyl sulfate.

16. The composition of claim 13 wherein the antigen is a viral antigen.

17. The composition of claim 16 wherein the antigen is rubella virus antigen.

18. The composition of claim 16 wherein the antigen is CMV antigen.

19. A process for producing a solid particulate support sensitized with a detergent-treated antigen, which is resistant to self-agglutination, comprising:

contacting an intracellular parasite antigen with a detergent and supporting the detergent-treated antigen on a solid particulate support.

20. The process of claim 19 wherein the solid support is a synthetic polymer.

21. The process of claim 20 wherein the synthetic polymer is selected from the group consisting of polyvinylchloride, polystyrene, aminated polystyrene and carboxylated polystyrene.

22. The process of claim 20 wherein the antigen is covalently coupled to the solid support.

23. The process of claim 20 wherein the antigen is adsorbed on the solid support.

24. The process of claim 23 wherein the antigen is a herpes virus antigen.

25. The process of claim 23 wherein the detergent is an alkali dodecyl sulfate.

26. The process of claim 23 wherein the antigen is a viral antigen.

27. The process of claim 26 wherein the antigen is rubella virus antigen.

28. The process of claim 26 wherein the antigen is CMV antigen.

* * * * *

The Constitutional Provisions
U.S. Code, Title 35, Patents
Index

THE CONSTITUTIONAL PROVISION

ART. 1, SEC. 8., CL. 8. The Congress shall have power . . . To promote the progress of science and useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries.

UNITED STATES CODE

TITLE 35—PATENTS

§ 100 Definitions

When used in this title unless the context otherwise indicates—

(a) The term "invention" means invention or discovery.

(b) The term "process" means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material.

(c) The terms "United States" and "this country" mean the United States of America, its territories and possessions.

(d) The word "patentee" includes not only the patentee to whom the patent was issued but also the successors in title to the patentee.

(July 19, 1952, ch. 950, 66 Stat. 797.)

§ 101 Inventions patentable

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

(July 19, 1952, ch. 950, 66 Stat. 797.)

§ 102 Conditions for patentability; novelty and loss of right to patent

A person shall be entitled to a patent unless—

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States, or

(c) he has abandoned the invention, or

(d) the invention was first patented or caused to be patented, or was the subject of an inventor's certificate, by the applicant or his legal representatives or assigns in a foreign country prior to the date of the application for patent in this country on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent, or

(f) he did not himself invent the subject matter sought to be patented, or

(g) before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

(July 19, 1952, ch. 950, 66 Stat. 797; July 28, 1972, Pub. L. 92-358, § 2, 86 Stat. 502; Nov. 14, 1975, Pub. L. 94-131, § 5, 89 Stat. 691.)

§ 103 Conditions for patentability; non-obvious subject matter

A patent may not be obtained though the invention is not identically disclosed or described as set forth in § 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of § 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

(July 19, 1952, ch. 950, 66 Stat. 797; Nov. 8, 1984, Pub. L. 98-622, § 103)

§ 112 Specification

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A claim may be written in independent or, if the nature of the case admits, in dependent or multiple dependent form.

Subject to the following paragraph, a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

A claim in multiple dependent form shall contain a reference, in the alternative only, to more than one claim previously set forth and then specify a further limitation of the subject matter claimed. A multiple dependent claim shall not serve as a basis for any other multiple dependent claim. A multiple dependent claim shall be construed to incorporate by reference all the limitations of the particular claim in relation to which it is being considered.

An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.

(July 19, 1952, ch. 950, 66 Stat. 798; July 24, 1965, Pub. L. 89–83, § 9, 79 Stat. 261; Nov. 14, 1975, Pub. L. 94–131, § 7, 89 Stat. 691.)

§ 154 Contents and term of patent

Every patent shall contain a short title of the invention and a grant to the patentee, his heirs or assigns, for the term of seventeen years, subject to the payment of fees as provided for in this title, of the right to exclude others from making, using, or selling the invention throughout the United States, referring to the specification for the particulars thereof. A copy of the specification and drawings shall be annexed to the patent and be a part thereof.

PATENT EXAMINING CORPS

RENE D. TEGTMEYER, Assistant Commissioner

JAMES E. DENNY, Deputy Assistant Commissioner

CONDITION OF PATENT APPLICATIONS AS OF August 15, 1987

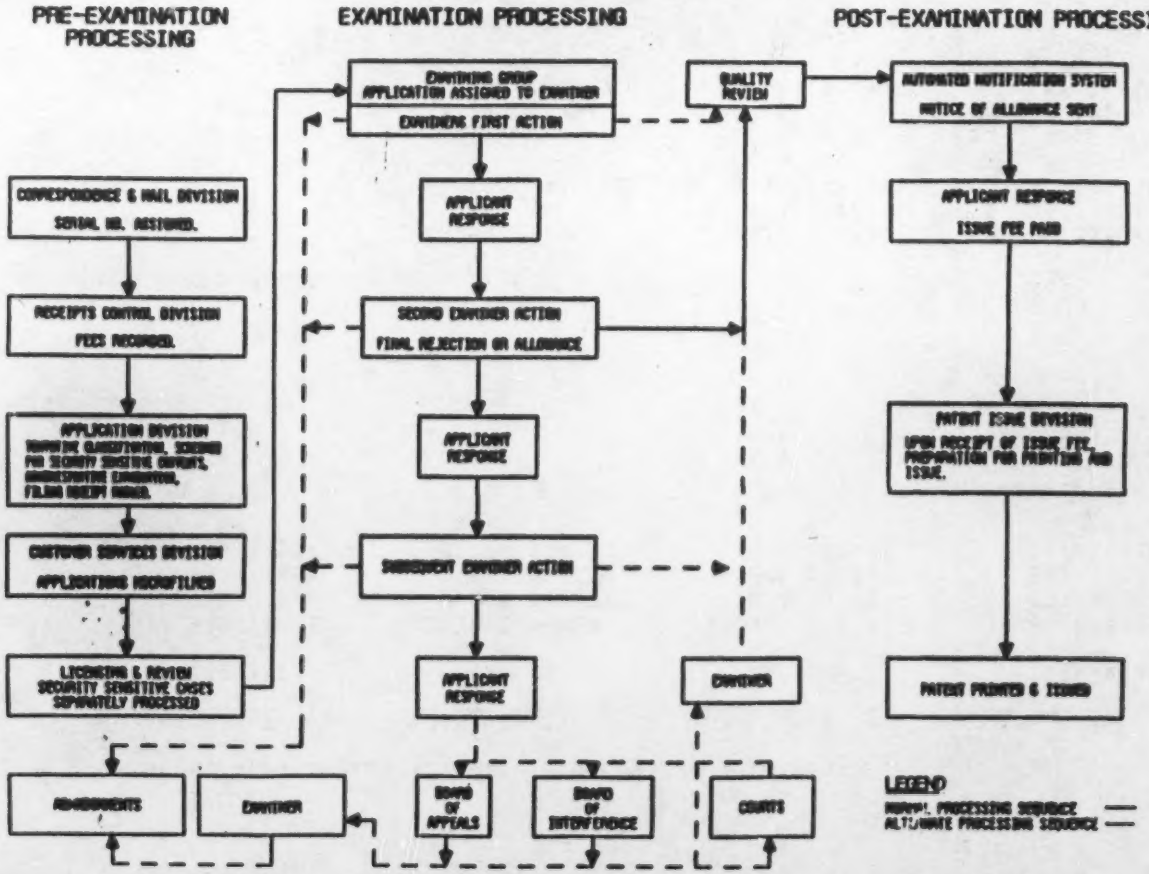
PATENT EXAMINING GROUPS	Actual Filing Date of Oldest New Case Awaiting Action
CHEMICAL EXAMINING GROUPS	
GENERAL METALLURGICAL, INORGANIC, PETROLEUM AND ELECTRICAL CHEMISTRY, AND ENGINEERING, GROUP 110—D. E. TALBERT, Director	5-13-86
ORGANIC CHEMISTRY AND BIOTECHNOLOGY, GROUP 120—C. E. VAN HORN, Director	2-15-85
SPECIALIZED CHEMICAL INDUSTRIES AND CHEMICAL ENGINEERING, GROUP 130—R. F. WHITE, Director	1-30-86
HIGH POLYMER CHEMISTRY, PLASTICS, COATING, PHOTOGRAPHY, STOCK MATERIALS AND COMPOSITIONS, GROUP 150—J. O. THOMAS, Director	1-29-86
ELECTRICAL EXAMINING GROUPS	
INDUSTRIAL ELECTRONICS, PHYSICS AND RELATED ELEMENTS, GROUP 210—G. GOLDBERG, Director	2-18-86
SPECIAL LAWS ADMINISTRATION, GROUP 220—K. L. CAGE, Director	7-30-85
INFORMATION PROCESSING, STORAGE, AND RETRIEVAL, GROUP 230—E. LEVY, Director	9-07-84
PACKAGES, CLEANING, TEXTILES, AND GEOMETRICAL INSTRUMENTS, GROUP 240—TRYGVE M. BLIX, Director	11-4-85
ELECTRONIC AND OPTICAL SYSTEMS AND DEVICES, GROUP 250—EDWARD E. KUBASIEWICZ, Director	8-16-85
COMMUNICATIONS, MEASURING, TESTING AND LAMP/DISCHARGE GROUP, GROUP 260—S. G. KUNIN, Director	7-10-85
DESIGN, GROUP 290—K. L. CAGE, Director	1-14-85
MECHANICAL EXAMINING GROUPS	
HANDLING AND TRANSPORTING MEDIA, GROUP 310—B. R. GRAY, Director	3-25-86
MATERIAL SHAPING, ARTICLE MANUFACTURING AND TOOLS, GROUP 320—S. N. ZAHARNA, Director	10-04-85
MECHANICAL TECHNOLOGIES AND HUSBANDRY PERSONAL TREATMENT INFORMATION, GROUP 330—R. E. AEGERTER, Director	10-15-85
SOLAR, HEAT, POWER, AND FLUID ENGINEERING DEVICES, GROUP 340—D. J. STOCKING, Director	5-28-86
GENERAL CONSTRUCTIONS, PETROLEUM AND MINING ENGINEERING, GROUP 350—A. L. SMITH, Director	10-01-86

Expiration of patents: The patents within the range of numbers indicated below expire during August 1987, except those which may have had their terms curtailed by disclaimer under the provisions of 35 U.S.C. 253. Other patents, issued after the dates of the range of numbers indicated below, may have expired before the full term of 17 years for the same reasons, or have lapsed under the provisions of 35 U.S.C. 151.

Patents ..... Numbers 3,522,401 to 3,526,003, inclusive

Plant Patents ..... Numbers 2,986 to 2,988 inclusive

THE PATENT PROCESS



Patent Application Activity - Group 120 (Biotech)

	AUG. 1987	JAN. 1987	JAN. 1986	JAN. 1985
Examiners	128 (42)	106 (31)	112 (32)	115 (28)
Pending Applications	18,858 (7821)	17,722 (5837)	17,968 (5773)	16,691 (3903)
New	8,711 (4388)	7,284 (3307)	7,014 (3155)	6,137 (2202)
Amended	902 (309)	1,662 (651)	1,645 (445)	637 (172)
Rejected	9,245 (3124)	8,776 (1879)	9,309 (2173)	9,917 (1529)
Pendency (Months)				
To 1st Action	10.5	9.6	9.1	9.3
Disposal	21.1	20.5	19.7	19.9
Issue/Abandoned	25.3	24.6	23.7	25.3

CALENDAR YEAR	1986	1985	1984
Total Completed	10,944 (2044)	10,836 (1573)	9,290 (1171)
Allowed	5,560 (816)	5,594 (712)	5,234 (556)
% Allowed	51% (40.0%)	52% (45.3%)	56% (47.5%)
Appeals	794 (105)	856 (84)	722 (91)
% Appealed	7.3% (5.1%)	8.0% (5.3%)	7.6% (7.8%)

Biotechnology in Pharmaceuticals: The Japanese Challenge

Mark D. Dibner

Summary. The products of biotechnology are being developed for new diagnostics and therapeutics, and it is predicted that they will have great impact on the pharmaceutical industry. In the United States, pharmaceutical companies are incorporating biotechnology into their research and development programs, often with the contractual assistance of small biotechnology firms. Their strongest competition is arising in Japan, where there are now concerted government and industry efforts to expand biotechnology capabilities and to optimize commercialization. Strategies used by the United States and Japan to incorporate biotechnology into their pharmaceutical industries are examined and compared.

The pharmaceutical industry in the United States has enjoyed steady growth and stability throughout most of this century. In 1984 the industry posted greater profit margins than any other industry group (*1*). However, the industry is also undergoing great change, largely because of biotechnology. The use of living cells to produce commercial products is having a major impact on the drug industry, with the anticipation of there being new products, new processes, new entrants into the industry, and increased competition.

Pharmaceutical companies are now taking action to address the impact of biotechnology. How they incorporate the new technologies and how they face new competition may play a significant role in defining their financial success in the future. Of the new forms of competition confronting U.S. firms, the strongest is projected to be from Japan (*2*, *3*). Current strategies used by U.S. and Japanese firms to incorporate biotechnology are the focus of this article.

Impacts of Biotechnology

Traditionally, pharmaceuticals have been manufactured through chemical synthesis or purification processes. Genetic engineering makes it possible to manufacture a host of new molecules with projected uses as therapeutic agents. Among those currently under development are the interferons, interleukins and other lymphokines, tissue and kidney plasminogen activators, and tumor necrosis factor. Other biotechnologically produced therapeutics, previously made by other methods, include human insulin, growth hormone, serum albumin, and clotting factor VIII. These proteins can be produced in abundance by genetic engineering techniques and may have fewer side effects than do proteins derived from nonhuman sources (*4*, *5*). Moreover, new processes can be employed to produce vitamins, amino acids, steroids, antibiotics, enzymes, bioactive peptides, and many other molecules for potential use as drugs, as well as novel compounds for use as vaccines (*6*, *7*). Products of hybridomas, such as the monoclonal antibodies, are already important for use in new, sensitive diagnostics. In addition, monoclonal antibodies with therapeutic uses are on the horizon. At present, insulin is the only therapeutic entity developed by biotechnology approved for human use in the United States. In comparison, approximately 100 monoclonal antibodies have been approved for use in diagnostics. Many additional compounds are in various stages of development or testing, and they should reach the marketplace within the next decade (*2*, *6*).

Another impact of biotechnology will be in pharmaceutical manufacturing. In many instances, it should be possible to produce molecules with higher purity, and perhaps more cheaply, through cell growth and fermentation processes (*2*, *5*–*8*). This will not be without cost; new production facilities must be built at an expense of up to $100 million each (*6*), and bioprocess engineering personnel must be trained or hired.

Most U.S. and foreign pharmaceutical companies are aware of the scientific and financial importance of biotechnology, and they are in the process of incorporating biotechnology skills into their programs and plans. In 1983 the worldwide market for pharmaceuticals was over $60 billion (*9*), and biotechnology may eventually affect the production of 20 percent of the current pharmaceutical products (*6*). In addition, sales of new drugs and diagnostics made possible by biotechnology are predicted to reach $10 billion within the next decade, and they should rise thereafter (*2*). With such large markets at stake, pharmaceutical companies in the United States are attempting to be strong competitors in biotechnology. But can these companies continue to enjoy profits and growth with new competition on the horizon?

Biotechnology Industry

Fermentation processes have long been in commercial use. In the early 1970's genetic engineering and hybridoma technologies were developed, primarily in academic laboratories (*2*, *5*). Subsequently, many small biotechnology firms were formed, often by academic scientists, to commercialize advances made in basic research (*2*, *5*). A 1984 compilation in *Genetic Engineering News* listed over 300 companies with major biotechnology efforts, the vast majority of the companies being small and recently formed (*10*). More than half of these new companies are involved in pharmaceutical or diagnostic development (*2*, *10*). More than 75 percent of these biotechnology firms worldwide have been formed in the United States, with an initial total investment of $2 billion to $2.5 billion (*3*, *7*, *10*). To provide a return on this investment, the new companies have entered into contract research, as well as the licensing of products they develop. Some are also attempting to directly market their products, but most do not have available the extensive resources necessary to take a pharmaceutical product through the regulatory process; nor do they have the necessary production or marketing expertise (*2*, *11*). Thus, much of the effort of these small firms can be described as technology transfer to larger companies.

An analysis of strategies used by pharmaceutical companies to incorporate

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biotechnology yields three categories: (i) academic relationships, (ii) internal expansion, and (iii) agreements with biotechnology firms (*12*). All three strategies are used by many companies but the most frequently used one is the third—agreements with biotechnology firms (*2*, *12*). Joint projects between large U.S. pharmaceutical companies and biotechnology firms (Table 1) should lead to the commercialization of a number of important products of biotechnology within the next decade (*2*, *12*).

New Competition

The U.S. pharmaceutical industry is comprised mostly of large, established companies that have been responsible for the development and introduction of many major drugs. As a result of biotechnology, there should be major changes in the composition of the industry in the form of new competition.

One major source of competition will be large, nonpharmaceutical firms that have planned a future in pharmaceuticals through biotechnology programs. Companies such as Monsanto and Du Pont, which currently have only modest sales related to pharmaceuticals, have announced major expansion of their drug and diagnostic research efforts with emphasis on biotechnology. Table 2 demonstrates that, in addition to drug companies, there are large, nonpharmaceutical companies that are also buying equity positions in biotechnology firms. The new technologies also are important for future products in the chemical industry; nine of the ten largest U.S. chemical companies have announced their involvement in biotechnology for the development of agrichemicals and pharmaceuticals (*13*). Large companies with current emphasis on chemicals, foods, textiles, and other goods could become prominent contenders in the pharmaceutical industry of the future.

A second source of competition will be from the biotechnology firms themselves. Although most do not have the capital to bring a drug to market, many of these firms do have the ability to market diagnostics. Through financial incentives, such as research and development limited partnerships (RDLP's), biotechnology firms may obtain the capital to directly market therapeutics in the future (*2*, *14*). In each year from 1982 to 1984, a total of $166 million to $199 million was raised by five to nine firms to form RDLP's that involve the development of specific biotechnology-based products (*14*).

Foreign Competition

The strongest source of competition in biotechnology for U.S. companies appears likely to come from abroad. Whereas the United States has no significant federal program for the coordination of biotechnology efforts, the governments of Great Britain, France, West Germany, and Japan have mounted major programs for the growth of domestic biotechnology (*2*). The country predicted to have the greatest potential impact on the commercialization of biotechnology is Japan (*2*, *3*). Although the new biotechnologies have been largely developed in the United States, the Japanese are expected to soon take the lead in commercialization of these technologies (*2*, *3*). A large part of their success will be based on products first developed in the United States. An analysis of Japan's incorporation of biotechnology may help in understanding this process.

Strategies Used by the Japanese

Historically, the Japanese pharmaceutical industry has been quite different than that in the United States, as is indicated in Table 3. Japanese drug companies are considerably smaller than their U.S. counterparts; there are 11 U.S. drug companies with annual pharmaceutical sales (1983) of over $1 billion, but only one Japanese company, Takeda, has reached that mark (*15*). In the past, U.S. companies were responsible for the introduction of twice as many new drugs as Japanese firms (*2*, *9*). In recent years, however, Japanese pharmaceutical companies have spent almost 50 percent more on research and development (as a proportion of sales) than U.S. companies (*1*, *9*). As a result, Japanese companies introduced 70 percent more new drugs between 1981 and 1983 than did U.S. companies (*2*). Given the total amount spent on research and development, the Japanese have been at least six times more productive (as measured by number of drugs introduced) per dollar spent on research (*16*). A recent estimate from the Japanese Bio-Industry Development Center predicts $60.7 billion in biotechnology-related Japanese sales by the year 2000, with $12.8 billion coming from pharmaceuticals (*17*), confirming Japan's emphasis on biotechnology.

Japan is considered a world leader in fermentation technology (*3*, *5*, *17*). This is of key importance to commercial success in biotechnology, but basic research is also necessary to supply new products for companies to market. Recent Japanese progress in biotechnology has resulted from coordinated efforts by the government, individual companies, and academic laboratories. Moreover, Japanese companies have received considerable foreign help, mostly from the United States, in filling certain gaps in basic research and development.

Japanese government programs in biotechnology have emerged from three sources: the Science and Technology Agency (STA), the Ministry of International Trade and Industry (MITI), and

Table 1. Joint projects between large U.S. pharmaceutical companies and biotechnology firms. Interactions announced between 1981 and 1984, selected from database (*12*). Two Swiss-based companies, Hoffmann–La Roche and Sandoz, that have major facilities in the United States are also included.

Biotechnology firm	Pharmaceutical company	Products involved
Biogen	Merck	Hepatitis B vaccine
	Schering-Plough	Interferon
	SmithKline	Anticlotting factor
Centocor	Abbott	Cancer diagnostics
	Hoffmann–La Roche	Monoclonal antibodies for cancer treatment
	Warner-Lambert	Hepatitis B diagnostics
Collaborative Research	Sandoz	Kidney plasminogen activator
Genentech	Hoffmann–La Roche	Interferons
	Lilly	Insulin
	Baxter Travenol	Diagnostics
Genetic Systems	Syntex	Diagnostics
Genetics Institute	Baxter Travenol	Factor VIII
Genex	Bristol-Myers	Interferons
Hybritech	Baxter Travenol	Monoclonal antibodies for bacterial infection
Molecular Genetics	Lederle	Herpes simplex vaccine

Table 2. Equity purchased in firms with a major focus on biotechnology. Equity purchases selected from database (*12*).

Large company (purchaser)	Biotechnology firm	Year
Purchased by U.S. pharmaceutical companies		
Abbott	Amgen	1980
Baxter Travenol	Genetics Institute	1982
Becton Dickenson	Applied Biosystems	1984
Johnson & Johnson	Enzo Biochem	1982
Lederle	Molecular Genetics	1981
Lederle	Cytogen	1983
Lilly	Synergen	1984
Schering-Plough	Biogen	1982
Schering-Plough	DNAX Ltd.*	1982
SmithKline	Beckman*	1982
Syntex	Genetic Systems	1982
Purchased by other U.S. companies		
Dow	Collaborative Research	1981
Du Pont	New England Nuclear*	1981
Fluor	Genentech	1981
W. R. Grace	Amicon*	1983
Martin Marietta	Molecular Genetics	1982
Monsanto	Biogen	1980
Monsanto	Collagen Corporation	1980
Purchased by Japanese companies		
Green Cross	Collaborative Research	1981
Mitsubishi	BioVec	1984

*Acquisition. Each nonacquisition purchase involved an average of $8 million.

Table 3. Comparison of U.S. and Japanese pharmaceutical industries and involvement in biotechnology. All 1983 data, except as noted. [Sources: (*1*, *2*, *9*, *15*)]

Data category	United States	Japan
Population (millions)	234.5	119.2
Gross national product	$3.3 trillion	$1.2 trillion
Domestic pharmaceutical market (world rank)	$21.3 billion (1)	$13.4 billion (2)
Number of pharmaceutical companies with sales over $1 billion*	11	1
Total pharmaceutical sales of ten largest pharmaceutical companies†	$16.7 billion	$6 billion
Pharmaceutical sales as percent of total sales‡	50.1	74.1
Number of new pharmaceutical products introduced:		
1961–1980	353	155
1981–1983	24	41
R&D expenditures as percent of sales‡	6.8	9.2
Scientists and engineers in industrial R&D§:		
Total number	573,900	272,000
Percent of work force	0.58	0.50
Government-funded research in biotechnology:		
Total	$520 million	$60 million
Percent of basic research	>98	<50
Targets of funding in biotechnology	Basic research	Basic research, scale-up, industrial projects, government laboratory facilities, manufacturing technology

*Pharmaceutical sales only. †Total world pharmaceutical sales in 1983 were approximately $60 billion. ‡Average of top ten companies. §All industries, 1977 data.

the Ministry of Agriculture, Forestry and Fisheries (MAFF) (*2*, *18*). The total government support for biotechnology, $50 million to $60 million in 1984, is only about one-tenth of that spent by the U.S. government (Table 3) (*2*, *18*), but Japanese funding is much more focused on specific projects. For example, MITI, in a 10-year strategic program beginning in 1981, has targeted next-generation technologies to foster scale-up techniques, aimed at assisting in the commercialization of biotechnology (*2*). The STA is also funding applied research, such as the development of bioreactors (*2*). The latest announced budgets of STA, MAFF, and MITI are emphasizing national centers related to biotechnology research, including the development of cell line and gene banks (*18*). Very little of the Japanese government's support for biotechnology is for basic research (*2*). In contrast, the U.S. government's support of biotechnology is almost ten times more, but support of applied research makes up only 1 to 2 percent of this total, with far less specificity than in Japan (Table 3) (*2*).

Another emphasis in Japan is to foster cooperation between companies and between industry and academia. There are more than a dozen joint ventures on record involving two or more Japanese companies that are aimed at developing therapeutics through research in biotechnology (*2*, *19*). Similar cooperation between large U.S. companies does not (or cannot) exist (*2*).

In order to further foster cooperation between Japanese companies, a trade association, tentatively called the Society for Advanced Pharmaceutical Research, was formed in 1985 with 31 member companies and the support of Japan's Ministry of Health and Welfare (*19*). A trade group, the Industrial Biotechnology Association, exists in the United States with 46 member companies, but is not supported by the federal government (*20*).

Because government funding in Japan is focused on applied research, Japanese companies are also in the process of expanding in-house expertise in basic research and development in biotechnology. Many companies have announced the expansion of research facilities, such as Sankyo's new $53-million biotechnology laboratory to be completed by 1986 (*21*). The availability of personnel to staff basic research laboratories in Japan has been a problem, primarily owing to a paucity of university programs in molecular genetics (*2*, *16*). To fill the need for researchers, some Japanese companies

have begun in-house training programs, while others have sent employees abroad to be trained or have hired foreign researchers (*2*).

These methods are apparently successful; the number of in-house scientists involved in basic research in biotechnology has increased more than fivefold in the past 3 years (*16*). Japan has an ample supply of fermentation process engineers, which is important for the commercialization of biotechnology (*2, 16, 22*). In contrast, in the United States the supply of basic researchers for biotechnology has not been as much of a problem, although it is expected that there will be a shortage of scientists trained in bioprocess engineering (*2, 16, 22*).

In Japan, little venture capital has been available and very few biotechnology firms have been formed (*2, 16, 23*). With in-house incorporation of biotechnology still at an early stage, Japanese companies have turned to U.S. biotechnology firms for basic research assistance. Table 4 identifies a number of these contractual agreements, some of which involve the same U.S. biotechnology firms and the same products as covered by agreements with U.S. pharmaceutical companies (see also Table 1). In most cases the contractual agreement gives the Japanese company licensing rights to a product developed in the United States, often with marketing rights being limited to Japan and other Asian countries (*2, 16, 24*). In only a few instances have Japanese companies purchased equity in biotechnology firms in the United States (Table 2).

To assess the extent of both domestic and foreign involvement with U.S. biotechnology firms, I have created a database of recorded pharmaceutical-related interactions between these firms and large companies (*12*). This database includes 72 joint or contractual interactions between U.S. biotechnology firms and U.S. companies from 1981 to 1985. Additionally, the database includes 43 such interactions between U.S. biotechnology firms and Japanese companies, 60 percent as numerous as those with U.S. companies (*12*). It is clear that Japanese companies, like large U.S. companies, are relying on contractual agreements with small U.S. firms to provide basic research or newly developed products (*2, 16, 25*).

Some U.S. biotechnology firms have set up facilities in Japan to coordinate joint research with Japanese companies. For example, Genentech Ltd. was set up in Japan in 1982 to serve as a liaison between Genentech in the United States and multiple Japanese firms with which it does business (*26*).

As has occurred in the United States, Japanese companies not previously involved in pharmaceuticals have started biotechnology programs that could lead to pharmaceutical products. A recent listing noted 10 major Japanese chemical companies, 13 food processing companies, and 4 textile companies that have biotechnology-related pharmaceutical projects (*2*). Most of these companies have contractual agreements with U.S. biotechnology firms (*12*).

In increasing numbers, large U.S. companies are forming joint subsidiaries with Japanese companies for the commercialization of pharmaceuticals, as evidenced by such company names as Merck-Banyu, Pfizer Taito, Nippon Upjohn and Du Pont–Sankyo (*15, 27*). Other joint agreements, not involving the formation of subsidiaries, have been recorded with U.S. pharmaceutical companies, such as Shionogi's agreements with Lilly and Merck (*12, 24*). In addition to U.S. companies entering Japan, at least one Japanese pharmaceutical company is setting up a biotechnology facility in the United States. Otsuka, Japan's fourth largest pharmaceutical manufacturer, is building a $7-million biotechnology research facility in Maryland, to be completed in 1985 (*28*). Other Japanese pharmaceutical companies already have or plan manufacturing facilities in the United States; they include Takeda, Japan's largest pharmaceutical company, which has a plan for a vitamin-production facility in North Carolina.

United States and Japan: Comparison of Strategies

In comparing the incorporation of biotechnology into the U.S. and Japanese pharmaceutical industries, some similarities are apparent. Companies in both countries have expanding in-house biotechnology efforts, but are also relying on the new biotechnology firms, primarily U.S. ones, to gain access to basic research in biotechnology and to obtain products for commercialization. This method appears successful; many initial products of these collaborations are in the pipeline for approval by the Food and Drug Administration (*29*). For example, human insulin, the first therapeutic developed by biotechnology, was evolved by Lilly in collaboration with Genentech; and alpha interferon, to be marketed by Schering-Plough, was developed by Biogen (*4, 6*).

In both countries there is new pharmaceutical industry competition attributable to biotechnology. Nonpharmaceutical companies, such as Exxon, Corning, W. R. Grace, Monsanto, Martin Marietta, and Du Pont, have planned major programs in biotechnology (*2, 12*). Giant Japanese corporations, such as Mitsubishi Chemical, Ajinomoto, Suntory, Kirin Brewery, and Asahi Chemical Industry also are in the process of developing pharmaceutical products employing biotechnology (*2, 12*). It is thus likely that the composition of the pharmaceutical industry in both countries will change radically over the next decade.

Where Japan and the United States

Table 4. Contractual agreements between U.S. biotechnology firms and major Japanese companies. Agreements announced between 1981 and 1984, selected from database (*12*). Abbreviations: HSA, human serum albumin; IL-2, interleukin-2; MAb, monoclonal antibodies.

Biotechnology firm	Japanese company	Products involved
Biogen	Shionogi	Interferon, IL-2, HSA
	Fujisawa	Tissue plasminogen activator
	Green Cross	Hepatitis B vaccine
	Suntory	Tumor necrosis factor
	Teijin	Factor VIII
Centocor	Toray	Hepatitis diagnostics
Collaborative Research	Green Cross	Urokinase, interferon
Genentech	Mitsubishi	Tissue plasminogen activator
	Toray	Interferons
Genetic Systems	Daiichi	Diagnostics for blood disorders
Genetics Institute	Chugi	Human erythropoietin
Genex	Yamanouchi	Fibrinolytic agent
	Green Cross	HSA
	Yoshitomi	IL-2
	Mitsui Toatsu	Urokinase
	Mitsubishi Chem.	HSA
Hybritech	Teijin	MAb's for cancer treatment
	Green Cross	Immunoglobulins
	Toyo Soda	MAb diagnostics

differ is in the type and amount of government support for the development of biotechnology. In Japan there is a clear effort by government to enhance the future commercial success of the pharmaceutical industry by assisting in the development of biotechnology. Although this support is administered by a few different agencies and is small in size (by U.S. standards), it is viewed both externally (*2*, *25*) and internally (*16*) as a single cohesive effort with a high potential for success. The companies involved must create their own basic research and development programs; government assistance is at the next level, helping to foster commercialization of products, manufacturing, and generic support, such as gene banks (*18*). In the United States, federal support for biotechnology is ten times greater in magnitude and is aimed at basic research. Although support of basic research programs in biotechnology should be continued and expanded to ensure maintained leadership in basic research, support for more applied areas is also needed (*2*, *16*).

Another contrast between the two countries is in the availability of basic researchers in biotechnology and bioprocess engineering. There was a reported shortage in the United States of basic researchers trained in genetic engineering, but this problem appears to have abated (*2*, *30*). Due to strong academic programs in this and related areas, the availability of basic researchers should continue to be sufficient (*2*). However, a paucity of academic programs in bioprocess engineering continues (*2*). As more companies generate products of biotechnology for scale-up, it is expected that there will be a severe shortage of personnel trained in production technologies, which may hamper commercial success (*2*). Japan has the opposite problem—an adequate supply of fermentation engineers but too few basic researchers with training in molecular genetics (*16*). This is another reason why Japanese companies have been borrowing U.S. basic research, but are predicted to outpace the United States in commercialization (*2*, *3*).

Outlook

In January 1984 the U.S. Congress Office of Technology Assessment (OTA) published a 612-page analysis on commercial biotechnology (*2*). The report noted the importance of biotechnology both for its basic scientific benefit and for its potential commercial development. In assessing the competitive position for the United States, the OTA report stated the following (*2*, p. 7):

> Japan is likely to be the leading competitor of the United States for two reasons. First, Japanese companies in a broad range of industrial sectors have extensive experience in bioprocess technology. Japan does not have superior bioprocess technology, but it does have relatively more industrial experience using old biotechnology, more established bioprocessing plants, and more bioprocess engineers than the United States. Second, the Japanese Government has targeted biotechnology as a key technology of the future, is funding its commercial development, and is coordinating interactions among representatives from industry, universities, and government.

When the focus of analysis is narrowed to the pharmaceutical industry, it can also be concluded that the Japanese have the potential to be a leading competitor. An important factor in their success has been the borrowing of basic biotechnological research by Japanese companies from U.S. biotechnology firms. Although biotechnology licensed by U.S. firms to Japanese companies generally involves marketing rights in Japan or Asia (*2*), the Japanese market for pharmaceuticals is the second largest in the world. When added to other Asian markets, it becomes two-thirds the size of the North American or European markets (*9*). U.S. pharmaceutical companies have gained 40 percent of their revenues from foreign sales, and the loss of a foreign market may represent lost income (*9*).

In addition to basic biotechnology borrowed from the United States, Japan has been simultaneously building its own strength in this field. There are more and more frequent reports of new developments in basic biotechnology and discoveries of new drugs from Japanese industrial laboratories (Table 3) (*12*). It is thus possible that Japan's predicted future strength in pharmaceutical biotechnology will come both from internal developments and strategic government programs (*16*).

This is not to imply that with Japanese strength in biotechnology will come U.S. weakness in this area. As stated earlier, pharmaceutical and other companies in the United States are expanding their efforts in biotechnology and are nearing their goals of bringing new therapeutics and diagnostics to market. However, an analysis of Japanese strategies may help to understand how U.S. industry can optimize this process. In addition, U.S. industry will be strengthened if the U.S. government makes the commercialization of biotechnology a high priority and funds specific academic and other programs leading to that goal (*2*). As stated in the OTA report (*2*): "The United States may compete very favorably with Japan if it can direct more attention to research problems associated with the scaling-up of bioprocesses for production."

In addition, government activities that enhance cooperation between companies, decrease regulation, or provide centers to assist in biotechnology would help meet this goal (*2*, *6*, *31*). However, in the period since the OTA report was made public, no broad program of support to strengthen the U.S. position in biotechnology has been announced by the federal government.

Steps in the Right Direction

A few recent developments should prove useful to the future development of biotechnology in the United States. The first is the opening of biotechnology centers to assist in the transfer of biotechnology expertise from academia to industry. Two of these centers are at Pennsylvania State University and in Research Triangle Park, North Carolina. The Penn State Biotechnology Institute has planned research and educational facilities and will allow member companies access to "application-oriented research" and to a pilot production facility for assistance in scale-up (*32*).

The North Carolina Biotechnology Center currently receives $2.5 million in annual funding from state, federal, and industrial sources. The center funds specific programs, such as its Monoclonal Lymphocyte Technology Center, which involves academic research at the University of North Carolina and Duke University, the participation of industry, and funding by the National Science Foundation. The five industrial members agree on priorities for directed research to be funded by specific grants to participating laboratories. Although still in its infancy, the Monoclonal Lymphocyte Technology Center is fostering cooperation between companies in a university environment that probably would not have otherwise occurred (*33*).

The Center for Advanced Research in Biotechnology (CARB), to be built in Gaithersburg, Maryland, will combine federal, state, county, and university efforts (*34*). With CARB, the National Bureau of Standards will add its analytical expertise to molecular biology expertise from the University of Maryland. A CARB research facility to be completed

in 1986 will house 130 scientists. In addition to basic and applied research in biotechnology, CARB will provide services to industry, including analytical measurements and molecular modeling on a supercomputer, and it will make available basic tools for research in biotechnology (*34*).

Lastly, the National Science Foundation has announced a $20-million, 5-year grant to establish the Center on Biotechnology Process Engineering at the Massachusetts Institute of Technology (*35*). This is part of a new program to advance engineering research with industrial applications. It is likely that industry will also provide support for this center (*35*). Although not part of a broad program to develop biotechnology, the creation of this center, CARB, and other biotechnology centers will greatly assist U.S. companies in developing the skills necessary to face competition.

Conclusions

The current situation involving biotechnology in the U.S. pharmaceutical industry and its competition can be summarized as follows: Many if not most of the significant advances in biotechnology over the past decade have occurred in academic laboratories in the United States. A large portion of this research has been funded by the U.S. government, currently at an annual rate of more than $500 million. As the commercial potential of the products of biotechnology has become apparent, these products and many of the researchers have been transferred to a new industry—the biotechnology industry. This fledgling industry has been formed with over $2 billion of venture capital, mostly from the United States.

A problem occurs with return on investment. The new biotechnology firms need income to remain in business, and, for the most part, they are not presently able to market their products directly. However, they can sell their research capabilities and rights to products.

The U.S. pharmaceutical industry will benefit greatly from these discoveries, but it does not have exclusive access. On the one hand, many other U.S. companies see this as an opportunity for future profits and a means to enter the pharmaceutical industry. On the other hand, many Japanese companies, poised with enormous fermentation expertise to commercialize the products of biotechnology, see this as an opportunity to buy products of basic research while developing basic research capabilities of their own. The investment to develop biotechnology has been made primarily in the United States, yet the commercial success of this research will be shared with companies from other countries, especially Japan. The dollars invested by the United States should lead to U.S. jobs and increased revenue for U.S. corporations, but some of that return will be lost. And Japan, with U.S. help, is predicted to soon become the leading competitor in this field.

It is not a question of whether biotechnology research should be supported; the benefits to mankind are large. However, the type of support can clearly affect the outcome. In addition to the continued support of basic research, a U.S. federal program needs to be strategically designed to foster academic, government, and industry programs that would lead to maximizing the commercial success of biotechnology within the United States. If this occurs, then the predicted future leader in both scientific advances and commercialization could be the United States. Without relation to defense, it is unlikely that the transfer of basic biotechnology will be highly regulated or curtailed in the future. However, it should be possible to borrow strategies from Japan for planning and coordinating the commercial success of technologies, present and future.

Biotechnology in the pharmaceutical industry is still at a very early stage. It may still be possible for U.S. industry to maximize the return on investment in basic research. New programs that emphasize shared knowledge and centralized facilities should assist industry in its ability to develop new therapeutics. Of key importance is the assistance provided by the federal government to optimize regulatory and financial environments and to furnish coordinated support for continued achievement in biotechnology research.

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(general)

Why the US should tackle today its crisis of tomorrow

Robert Marges looks at problems facing America's biotechnology industry

THE US semiconductor industry is in such and shape that many observers believe only the Government can save it, either through direct (defence) subsidies or by waiving antitrust enforcement via approval of the Sematech proposal, which would unite the industry in a huge joint research and development effort. Among the reasons for the crisis, it is suggested, are aggressive Japanese pricing strategies ("dumping" according to some US companies); superior institutional co-ordination between the Government and private firms in Japan; and flat out superiority in semiconductor manufacturing technology.

It may or may not be too late for US chip manufacturers. But what lessons does the semiconductor story hold for the future of other industries based on key new technologies, like biotechnology?

Biotechnology might seem like a completely different business, and it is in many ways. However, there are important parallels which bear examination. First, biotechnology is like the semiconductor industry in that US companies are proving to be the new product innovators, just like Bell Labs and Texas Instruments in the early days of semiconductors.

US manufacturers are churning out new products, ranging from pharmaceuticals to re-engineered seeds for staple crops. This is of course essential: you cannot have an industry without products. But while new-product research has grown strongly in the 1980s, according to a recent article in BioEngineering News, research and development spending on new process technologies has increased at a much slower rate.

Meanwhile, the Japanese, already among the world leaders in the closely-related field of fermentation technology, are characteristically placing a good deal of emphasis on process technologies, just as the Japanese semiconductor firms did in the 1970s.

Observers report that although US companies hold a big lead in basic science and new products, Japanese companies are ahead in applying new "bioprocess" techniques to a wide range of manufacturing tasks in the chemical, food processing, and waste processing industries.

As with semiconductors, the Ministry of International Trade (Miti) has actively encouraged companies to develop expertise in process technologies. (There are some indications, however, that the diffuse nature of the biotechnology "industry" — actually a collection of technologies — poses a more daunting challenge to Miti than semiconductors did.)

The parallels are not coincidental, of course. They reflect the basic (and highly successful) strategy of Miti and Japanese companies in technology-intensive industries — focus on manufacturing and process technologies.

> **Whatever form a bioprocess initiative takes, the message of the semiconductor debacle must be kept clearly in mind**

Seeking to avoid a replay of the semiconductor situation, it might be asked, "how does the strategy of the US Government and private companies compare?

The answer at this point would have to be "not very well."

In the US, the infant bioprocessing industry has shown mixed results so far. Some small companies have faced major difficulty adapting existing technologies to the astonishingly complex task of growing large numbers of cells in controlled culture environments. Others have done better, and a certain amount of venture money has found its way into the smaller businesses. Large companies like Genentech reportedly have made some advances in the process area, but these in-house advances by large firms will be unavailable to new entrants with promising product ideas in the absence of licensing agreements with the larger companies.

And overall, the level of venture capital funding for process technologies is quite low relative to that for new products.

The uncertainty and long-term nature of new process technologies appears to deter private investment. Understandably, federal funding—the typical solution to this form of "market failure"—is also inadequate. This is because the National Institutes of Health, the major source of research funds in biotechnology, is primarily concerned with the basic science that leads to new drugs and therapies. Manufacturing technologies were not even considered relevant to the NIH's work until the recent initiation of the Small Business Innovation Research Grant Programme, which sets aside five per cent of NIH funds for commercialisation projects.

In any event, the SBIR programme seems too small, and too unrelated to NIH's primary goals and expertise, to provide the high degree of stimulation and co-ordination that bioprocess research requires. A more specific, well-organised, and better funded initiative seems imperative if the US is to avoid the mistakes made in semiconductors.

It does not really matter which federal agency serves this function. The Department of Energy, with its long history of expertise in chemical engineering, is one possibility, as are the National Laboratories like the Lawrence Berkeley Laboratory.

Universities can help, too. But first, the age-old barriers between engineering departments and biology and chemistry departments must be broken, for example by the establishment of a cross-disciplinary major in biochemical engineering.

Whatever form the bioprocess initiative takes, the message of the semiconductor debacle must be kept clearly in mind.

If no action is taken, Americans may well be wringing their hands in a few years, trying to figure out how to salvage another key industry, born and nurtured in the US, but lost to countries which had the foresight to focus on manufacturing processes.

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Japan

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isation has also been strongly stimulated by biotechnology. The Ministry of International Trade and Industry (MITI) is the main funding agency, and it allotted a total of approximately U.S.$41.7 million to biotechnology-related activities in Fiscal Year (FY) 1987 [based on 135 yen = one U.S. dollar]. The total amount of the requested budget for FY 1988 shows only a small increase ($42.5 million). A portion of the budget is shown in *Table 2*.

Two trends should be noted. First, one of the highest priorities for funding is the Research and Development of Basic Technologies for Future Industries—this would include those activities that are on the "cutting edge" of new technology, such as recombinant DNA, large-scale production of tissue culture cells, bioreactors and bioelectronics (biochips).

Second, increased funding in 1988 will go to the Human Frontier Science Program (HFSP), a new project where the goals are to discover how living organisms function, with an emphasis on the brain, and to apply the results to electronics, food and other industries. In contrast to the rest of the budget, HFSP is viewed as an international effort, and researchers from around the world are expected to take part.

Following MITI's lead, other agencies in the government have begun funding biotechnology (in some cases the goals overlap). These organizations, and their 1987 bioscience budgets, which are not limited to biotech, are the Science and Technology Agency (STA)—$94.8 million; Ministry of Health and Welfare (MHW)—$29.6 million; the Ministry of Agriculture, Forestry and Fisheries (MAFF)—$43.7 million; and the Ministry of Education (MOE)—$37 million.

The funds are distributed both to private industries, universities and to research institutes. If patentable discoveries emerge from these projects, the government has the patent right and any company can apply for licensing.

Analysts in Japan note that MITI funding is about 1/10 that of the NIH in the U.S. More difficult to gauge, however, is how effectively the funds are being focused and utilized in each nation. For example, Japanese government funding for microelectronics historically has been much less than U.S. funding, yet the Japanese have had stunning triumphs in that market. ■

Recent Developments in the Patenting of Biotechnology in the United States

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Symposium on the Protection of Biotechnological Inventions

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Recent Developments in the Patenting of Biotechnology in the United States

Staff and Patent Application Activity

	January 1987	January 1986	January 1985
Examiners	31	32	28
Pending Applications			
New	3307	3155	2202
Amended	651	445	172
Rejected	1879	2173	1529
Total	5837	5773	3903
CALENDAR YEAR	1986	1985	1984
Applications Allowed	816	712	556
Total Completed	2044	1573	1171
% allowed	40.0%	45.3%	47.5%
Appeals	105	84	91
% appealed	5.1%	5.3%	7.8%

Patentable Subject Matter

Ever since the Supreme Court decision in Diamond v. Chakrabarty, 447 U.S. 303(1980) held that microorganisms produced by genetic engineering are not excluded from patent protection under the general patent statute (35 USC 101), it was clear that the question of whether or not an invention embraces living matter is not relevant to the issue of patentable subject matter. The principle consideration is whether the living thing is the result of human intervention.

The position of the Office with respect to products of nature is that the public should be free to use things that are found in nature. Thus, if an article or composition of matter occurs in nature it is not considered to be patentable subject matter under our general patent statute unless it is given a new form, quality, properties or combination thereof not present in the original article. A critical aspect of this issue is whether the article or composition of matter which might be considered to occur in nature has been changed or altered substantially. Purification has been held to be a basis of substantial change in the characteristics, functions or activity of a naturally occurring material to warrant patentability. The initial burden is on the examiner to show that a claimed product is likely to exist in nature as a result of natural processes.

The protection of plant life is now capable of protection under three separate laws. The 1930 Plant Patent Act (35 USC 161-164) for an asexually reproduced plant except a tuber propagated plant, generally follows the requirements of the general patent law except that the description of the invention need only be as complete as is reasonably possible. There are now almost 6000 plant patents that have been granted under the Plant Patent Act and are now being granted at a rate of almost 400 per year. The 1970 Plant Variety Protection Act is directed to sexually reproduced plants and is administered by the Plant Variety Protection Office in the Department of Agriculture. A patent-like Certificate is granted for a period of eighteen years. This certificate gives the owner the right to exclude others from sexually multiplying, using, selling, importing or exporting the protected variety in the United States, but also has several exemptions (e.g. farmer's crop exemption, research exemption, and compulsory licensing) which have no direct counterpart in the general patent law. About 2000 Plant Variety Protection Certificates have been issued, and are now being issued at a rate of about 200 per year (30% vegetables). Almost two years ago, the PTO Board of Patent Appeals held (Ex Parte Hibberd, 227 USPQ 443 (1985)) that plant subject matter in the form of plants, seeds, and tissue cultures were patentable subject matter under the general patent statute (35 USC 101). Protection under the general patent statute is available to an inventor even though the subject matter falls within the scope of protection afforded by the Plant Patent Act or the Plant Variety Protection Act. It is even conceivable that multiple forms of protection could be granted on the same plant invention so long as some provision is made to prevent extension of the exclusionary rights which are granted under each system and so long as there exists common ownership of the exclusionary rights.

The April 3, 1987 decision by the Board of Patent Appeals and Interferences (Ex Parte Allen) held that the claimed polyploid oysters are manufactures or compositions of matter within the scope of 35 USC 101. This reverses a long-standing policy of the PTO that multicellular animals per se did not constitute patentable subject matter under the general patent law.

The Allen application contained claims to a method of producing polyploidy in oysters which results in increased growth. The examiner determined that the process was patentable. The application also contained claims directed to a polyploid Pacific oyster produced by the method defined in the patentable process claims. The examiner had rejected these claims on two separate grounds of rejection: (1) 35 USC 101 - the claimed oysters were not patentable subject matter; and (2) 35 USC 103 - the claimed oysters were obvious over a printed publication that taught that it was known to chemically treat an American oyster to induce polyploidy as a way to increase growth. The Board reversed the first rejection, but agreed that the claimed oyster was not patentably different from the polyploid oysters taught in the prior art.

In reversing the rejection under 35 USC 101 the Board relied on observations made by the Supreme Court in the Diamond v. Chakrabarty decision. These observations included that the use of expansive terms "manufacture" and "composition of matter" modified by the comprehensive "any" in 35 USC 101 indicated that Congress "plainly contemplated that the patent laws would be given wide scope." The Supreme Court also had noted that the legislative history of §101 supports a broad construction and concluded that the committee reports accompanying the 1952 Act that Congress intended statutory subject matter to "include anything under the sun that is made by man." Finally, it should also be noted that the Supreme Court observed that the relative distinction regarding the scope of the general patent law was not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions. On April 7, 1987 the Commissioner of Patents and Trademarks signed a policy statement which is included at the end of this paper which defines in broad terms the policy that the Patent and Trademark Office will follow as a result of the Allen decision.

As you would note from that notice, this decision is not considered to disturb or alter the practice and policy of the Patent and Trademark Office that products found in nature will not be considered to be patentable subject matter under 35 USC 101. Although the PTO now considers nonnaturally occurring multicellular living organisms, including animals, to be patentable subject matter within the scope of 35 USC 101, the issue will arise as to whether a claim directed to or including within its scope a genetically modified human being will be considered to be patentable subject matter. The position of the PTO is that the grant of a limited, but exclusive property right in a human being is prohibited by the Constitution. While there may be other ways to exclude a human being from the scope of a broad claim directed to mammals, for example, one clearly appropriate mechanism would be to use the negative limitation "non-human" to exclude a human being from the scope of a claim and avoid a rejection under 35 USC 101.

We have estimated that there are about 15 applications pending with claims directed to animals per se. To the extent that such claims are directed to non-human nonnaturally occurring manufactures or compositions of matter - a product of human ingenuity, such claims will not be rejected under 35 USC 101 as being directed to non-statutory subject matter. Patents claiming new animals will be classified in class 800 - which is directed to multicellular living organisms. This class will also be original classification for most of the plant patents which are granted under 35 USC 101.

Application Disclosure Requirements

The application disclosure requirements for inventions related to biotechnology are the same as those for any other type of technology. There are three separate and distinct requirements that must be satisfied with respect to the claimed invention; (1) description requirement; (2) enablement requirement-or how to make and use the invention; and (3) best mode requirement.

The function of the description requirement is to insure that applicant had in their possession, as of the filing date of the application, the specific subject matter claimed by them. Although the law requires a written description of the invention, where the invention relates to living subject matter (unless the invention can be described by words only or relates to biological matter which is known and readily available) a deposit of the living subject matter may be required to satisfy this requirement.

The second requirement is that of enablement-how to make and use the claimed invention. The essence of this requirement is whether the disclosure contains sufficient teaching regarding the subject matter of the claims so as to enable one skilled in the pertinent art to make and use the claimed invention. One of the most prevalent standards for measuring sufficient enablement is whether there is sufficient working procedures in the application for one skilled in the art to practice the claimed invention without undue experimentation. A few decisions have applied this test to inventions concerning microbiology.

In Ex Parte Jackson, 217 USPQ 804 (Board of Appeals 1982) antibiotic was produced by fermentation using a newly discovered natural microbe. Some strains of the microbe were deposited, and others were not. The PTO Board of Appeals found that claims detailing the actually deposited microbes were allowable, broader generic claims to the newly developed genus and species were not. It reasoned that undue experimentation was required to discover other species of the invention that were not deposited, and were capable of producing the novel antibiotic, even in view of the taxonomic functional characteristics described in this specification.

In another case dealing with natural microbe, it was held that a deposit was not necessary to establish enablement. Tabuchi v. Nubel (194 USPQ 521). The issue in Tabuchi was whether the verbal description of certain yeast strains as belonging to a "citric acid accumulating, and hydrocarbon assimilating strain of yeast belonging to the genus Candida" was sufficient to enable the making and using of such strains for the production of citric acid. No deposit had been made, but it was determined that a large variety of yeast of the genus Candida were available through existing depositories and that only routine screening procedures were involved to determine whether they possess the desired property. This did not amount to undue experimentation, according to the Court, which held that a deposit was not necessary to provide enablement.

The issue of what is "undue experimentation" in biotechnology has received further analyses in the decision Ex Parte Forman, 230 USPQ 546 (Board of Appeals 1986). The invention in the Forman application was defined by two sets of claims. The first set was generic to hybrid bacteria comprising both their own typhoid antigens and foreign, non-typhoid antigens. These claims contain no reference to any deposit. The second set of claims were limited to certain specific hybrid bacteria on deposit. The examiner allowed the claims including a specific reference to a deposit. The examiner, however, had rejected the claims with no specific deposit and the Board of Appeals affirmed this rejection.

The Board summarized 8 factors to be considered in a determination of "undue experimentation":

A. Quantity of experimentation necessary
B. Amount of direction or guidance presented
C. Presence or absence of working examples
D. Nature of the invention
E. State of the prior art
F. Relative skill of those in the art
G. Predictability or unpredictability of the art
H. Breath of the claims

The Board acknowledged in this case that the level of skill in the art of molecular biology is high, but also observed that experiments in genetic engineering produce unpredictable results. In this case it was noted that there was no evidence to show how much effort it would take to isolate strain used to hyperconjugate the original strains in order to prepare the hybrids or whether there were a good screening method available to identify useful strains among the myriad of strains that were presumably produced. It was acknowledged that it would take about one year to construct most strains according to this invention. Although the Board indicated that the amount of time alone was not determinative of the issue of undue experimentation, it concluded that the disclosure lacked the guidance leading to predictability and found that the practice of the subject matter defined in the rejected claims would require undue experimentation.

Finally, the best mode requirement is a separate and distinct requirement from the enabling requirement. It is essentially an issue of concealment. In the absence of evidence of concealment (accidental or intentional) the patent examiner will assume that the best mode requirement has been satisfied. If the best mode contemplated by the inventor at the time of filing the application is not disclosed, such a defect cannot be cured by submitting an amendment seeking to put into the specification something required to be there when the patent application was originally filed. In the recent Hybritech case, the Federal Circuit found that the only evidence even colorably relating to concealment was testimony that competent people perform the screening and that the screening process is labor-intensive and time consuming. However, the Court found that it was not plausible that this evidence amounted to proof of concealment of a best mode for screening or producing Monclonal Antibodies for use in the claimed process.

Deposits

It is now clearly recognized that when a invention relates to a new biological material, the material may not be reproducible even when the detailed procedures and a complete taxonomic description are included in the application. Deposits may be used to satisfy one or more requirements of the application disclosure where the written description itself is not sufficient or where the invention cannot be practiced using known and publicly available biological material. What must be deposited if any deposition must be made for the U.S. patent application is that which is necessary to place the public in possession of the patented invention upon issuance of the U.S. patent. The question of the availiabilty of the starting materials or the final product is important in the context of whether there exists a reproducible technique to create either one from readily available starting materials. The necessity for depositing various types of biological material may be substantially eliminated as technology develops and more knowledge exists on the basic nature of these biological materials and how to manipulate them in a reproducible manner. What requires undue experimentation today, may in the future become merely routine and predictable.

The existing operating guidelines for patent examiners on the deposit of biological materials for patent purposes appears in the Manual of Patent Examining Procedure in §608.01(p), as modified by the decisions in In re Lundak, 227 USPQ 90 (Fed. Cir. 1985). While other arrangements may be suitable, it will be sufficient if a statement is made by applicant, an attorney prosecuting the application or a person representing the assignee that a deposit has been accepted under the Budapest Treaty under conditions that all restrictions on the availability to the public of the deposit will be irrevocably removed upon the granting of the patent.

This would mean that a viable deposit has been made (Rule 10) in an acceptable depository (IDA) for a period of five years after the most recent request and at least 30 years from the date of deposit (Rule 9) under conditions that access to the deposit will be available during pendency of the patent applicaton to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 USC 122 (Rule 11.1), and all restrictions will be removed once the patent is granted. Assurance of permanent availability of the deposited material through the depository is reasonably assured through the deposit of a viable culture under the Budapest Treaty. The PTO is presently working on an advanced notice of proposed rulemaking which will require clearance at the Department of Commerce before publication.

The proposed regulations will define the biological material which is subject to those regulations in an open-ended manner that will include material that is capable of self-replication, either directly or after insertion into a host. We will probably ask for some assistance in defining, for example, an appropriate number of seeds that would be required to be on deposit at the time the patent is granted. The rules will also attempt to

define when a deposit is required in the sense that the mere reference to a specific organism or other biological material in a specification disclosure will not create any presumption that the specific material is necessary to satisfy one or more of the requirements of §112. If the examiner determines that a specific material is necessary, a deposit will not be required if the material was known and readily available to the public or could be made or isolated in a reproducible manner from known and readily available material. We will attempt to define some of the factors that can be utilized in showing that a specific material is known and readily available. Among these factors would be the availability of the material from commercial suppliers or evidence of widespread distribution to those working in the art to which the invention pertains.

Among the acceptable depositories would clearly be the International Depository Authorities recognized under the Budapest Treaty. The recognition of depositories other than an IDA represents a problem for the PTO in determining the adequacy of the staff and facilities to preserve the deposit under the terms and conditions that would apply to IDA's. There may be an opportunity here for some consultation with industry groups for the determination of the suitability of a depository.

The proposed rules will provide for an opportunity for replacement or replenishment of a deposit where the orginial deposit is determined to be no longer viable, will probably provide for the supplementing of an original deposit (not replacement) in situations where the original deposit is contaminated or will no longer function in the manner which is alleged to characterize the original deposit. The original deposit in these circumstances would not be destroyed or replaced since it would provide the best evidence of the character and identity of the original deposit. Replacement in a different depository would also be permitted in circumstances where the original depository defaults in the services it is required to perform.

The term of a deposit will be for a period of a least five(5) years after the most recent request for the furnishing of a sample of the deposited biological material and for a term of at least 30 years after the date of deposit. According to the Board of Patent Appeals decision in Lundak, the availability of the deposited biological material which is essential for the making and/or using of the subject matter claimed in the patent beyond the enforceable life of a patent is a legitimate ground for concern on the part of the Patent and Trademark Office. It is not believed that the period set forth in the Budapest Treaty was intended to permit a situation where the biological material would not be stored beyond the enforceable life of the patent.

We intend to propose a requirement for viability at the time of deposit since experience has shown that many of the materials that are tested on deposit are not viable when received at the depository.

The PTO will require that all restrictions on the availability biological material will be irrevocably removed at the time of the patent grant. We intend also to solicit comments on the advisability of seeking legislation that would permit, for example, limitations on the access to such material and further transfer to third parties or countries which do not provide adequate protection for the technology embodied in the biological material on deposit.

Since the decision in Lundak, the deposit need not be made before the effective filing date in the United States. We will permit a deposit to be made up to the time the issue fee is paid in an application. If there is any disagreement between the examiner and the applicant with regard to whether a deposit is required, or the conditions under which it will be deposited, the examiner will make and maintain a rejection under 35 USC 112, first paragraph. In those situations where the application is incondition for allowance except for the actual deposit in a suitable depository, the examiner will allow the application, mail the Notice of Allowance and Issue Fee Due, and simultaneously require that the deposit be made before payment of the issue fee. This will also require an amendment under 37 CFR 1.312 to complete the description of the accession number and depository in the application specification. The specification should also include a written description of the biological material which is sufficient to identify and characterize that material. This description is desirable not only from the standpoint of examination, but also from the standpoint of using this particular disclosure as prior art.

The determination of foreign priority rights will be determined on the basis of whether the application in the country foreign to the United States would be considered to be regularly filed. Thus, most countries foreign to the United States require that a deposit be made prior to the time of filing, whereas the United States permits a deposit to made subsequent to the filing date but before the patent is granted. This issue may also arise where an applicant in a country foreign to the United States applies for a breeder's rights certificate for a plant variety and decides to seek a utility patent under 35 USC 101 in the United States.

Several issues have arisen and will continue to arise directed to the deposit issue. It may be a question of judgement as to whether a deposit is required in any particular fact circumstances. This could arise from a situation as to whether the knowledge and skill in the art is sufficient to reproduce the claimed invention without undue experimentation, or whether the biological materials necessary are known and readily available to the public. Another issue in the deposit area is whether an applicant may act as their own depository even after the patent is granted so long as they provide the same assurances that must be met by a permanent depository according to the Office guidelines. Finally, the Office is considering the issue of what must be deposited in the context of a patent application claiming a

Monoclonal Antibody, where the antibody is deposited in a patent depository inaccordance with our guidelines, but the hybridoma source for the antibody is separately deposited under procedures and conditions that would not make it publicly available until the expiration of the U.S. patent. The hybridoma source would be available for replenishment of the antibodies to assure continued availability of the antibodies during pendency of the application and to the public during the term of the patent. The Office has taken the position that this creative scheme is not sufficient to satisfy the requirement that the disclosure provide a description on how to make the claimed antibody.

Non-Obviousness

The determination of non-obviousness (35 USC 103) is a mixed question of fact and law. The legal conclusion of obviousness or non-obviousness of a claimed invention is based on four(4) factual inquiries: (1) scope and content of the prior art; (2) differences between the prior art and the claimed invention; (3) the level of skill in the art to which the invention pertains; and (4) evidence of secondary considerations such as commercial success, unexpected results, or long-felt need. The patent applicant has the opportunity, through Information Disclosure Statement or Affidavits/Declarations to timely provide factual evidence directed to any or all of these factual inquiries for consideration by the patent examiner and any reviewing authority.

The analytic approach to a determination of obviousness is the same regardless of type of invention is being considered. The facts relied upon by the examiner generally must be derived from evidences known and accessible to the public at the time prior to applicant's invention or the filing date of the application.

The decision in Ex Parte Old, 229 USPQ 196 (Bd. of Appeals 1985) deals with hybridoma technology and the level of inventive skill required to establish unobviousness. The claims were limited to exemplified Monoclonal Antibodies and the examiner had established that polyclonal Antibodies which reacted with the cell-surface antigens were known. The analytic limitations of polyclonal antibodies were recognized and the cell antigens used to prepare antibodies were also known. It was the examiner's position that it would have been obvious to employ the Kohler and Milstein methodology to prepare monoclonals to the antigen. The majority opinion in this decision determined that hybridoma technology was an empirical art in which the practitioner is unable to foresee what particular antibodies will be produced and which specific surface antigens will be recognized by them. Further, the Board found that the examiner failed to establish that the character of the claimed Monoclonal Antibodies could be predicted or expected. In another as yet unpublished but related Board decision (Erlich) also dealing with hybridoma technology, the Board found that the level of skill to be such that once the antigen of interest is selected, the use of that antigen in the known method of Kohler and Milstein will result in the expected

hybridoma and the specific Monoclonal Antibodies. In this particular decision the Board concluded that the claimed Monoclonal Antibodies, cell line and method for producing Monoclonal Antibodies were obvious because one of ordinary skill in the art would had been motivated to produce Monoclonal Antibodies specific for the defined antigen using the method of Kohler and Milstein with reasonable expectation for success.

Patent Term Restoration

On September 24, 1984, the Drug Price Competition and Patent Term Restoration Act became law. It was designed to restore, to some extent, the reduction of the effective market life of a patent because of delays in the Federal regulatory review process through an extension of the patent term. The objective was to restore the diminished stimulus to innovation and research brought about by a decrease in the effective market life of a patent. The law provides that a patent may be extended for a period of up to five years if the patented drug, medical device, food additive or color additive has undergone regulatory review, but only two years if the patent was involved in the regulatory review process at the time of enactment of the law. In addition to the five year cap, in no case can the period of patent extension, when added up to the patent life left after approval of the product, exceed fourteen years.

The Office has received its first application for patent term extension of a biotech product - generic name MUROMONAB-CD3. The approved product is a murine monoclonal antibody to class CD3 antigen. The period of regulatory review was 812 days and the requested period of the patent term extension is 201 days. The law also provides for special treatment of a process patent which primarily uses recombinant DNA in the manufacture of the approved product. The law established separate rules for process patents which primarily use recombinant DNA because it was believed that such a new and important innovation should be rewarded, but that the discovery of other processes which do not utilize recombinant DNA as the essential and predominant technique do not warrant the same treatment as does the discovery of a new product.

Conclusion

In summary, the volume of patent application activity continues to be heavy and is leading to an increasing number of issued patents. The development of the law as it relates to the patenting of biotechnology inventions is in its infantcy, but hopefully it will be developed in the future in an orderly manner that will give rise to greater predictability in the granting and enforcement of patent rights. The Patent and Trademark Office is dedicated to make the patent system work to promote the progress of this young biotech industry in an environment where research and developement will be fostered.

FOOD DRUG COSMETIC LAW JOURNAL 42, 500–515 (1987)

Biotechnology Litigation and Federal Regulation: Status and Implications

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The commercial development and distribution of biotechnology-derived products has required the federal agencies responsible for regulating such products to design and implement formal and informal regulatory policies to permit considered, but not unduly burdensome, regulation of such products. Contrary to widespread initial belief, this task has proven to be more difficult than the formulation of policy concerning conventionally-derived products because of a significant and fundamental difference in perception with respect to the appropriate focus of the regulation of biotechnology. While the relevant federal agencies have focused their regulatory efforts to this time on the end products of biotechnology, public concern, and litigation challenges, have been focused on the process of biotechnology and its potential environmental effects. These conflicting focuses have provided the foundation for a still-unresolved struggle over the proper scope and direction of federal biotechnology regulation.

Prior to 1983, there were few regulatory developments with respect to biotechnology. Public participation in, or comment regarding, the development of regulatory policies with respect to biotechnology was limited, and scientific research and development proceeded with relatively little regulatory intervention. However, two recent significant developments, the publication of the Coordinated Framework for the Regulation of Biotechnology[1] and the commencement of litigation concerning the establishment of federal biotechnology programs and the testing and approval of biotechnology products, have accelerated the regulation of products derived from biotechnology.

In our view, the significant possibility of litigation concerning some aspects of the development or introduction of biotechnology-derived products must be taken into account, by both government and industry, at the earliest development stages and throughout the regulatory review process. Failure to attend prudently to the possibility of such litigation has, and will, unnecessarily delay and perhaps, on occasion, prevent product introduction and marketing.

The principal new regulatory developments concerning the approval of bio-

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[1] 51 Fed. Reg. 23,301 (1986) (hereinafter Coordinated Framework).

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technology products have been well-summarized recently[2] and, accordingly, we will only briefly review and update them. We will then discuss in detail the status and implications of the increasing amount of litigation related to the regulation of biotechnology. Finally, we will discuss certain of the significant unresolved regulatory issues which may be the subject of future litigation.

REGULATORY FRAMEWORK FOR REVIEW AND APPROVAL OF BIOTECHNOLOGY-DERIVED PRODUCTS

In June 1986, the White House Office of Science and Technology Policy published its Coordinated Framework for the Regulation of Biotechnology.[3] The Coordinated Framework presents the structure and general procedures for federal regulation of biotechnology, maintaining the view that existing statutes and divisions of authority among federal agencies provide a basis of agency jurisdiction over both biotechnology research and products sufficient to assure reasonable safeguards for the public. Two principal policies are established in the Coordinated Framework statement. The first is that the existing statutory frameworks, administered by the various relevant federal agencies,[4] are appropriate for regulating biotechnology-derived products. At the same time, however, the Coordinated Framework also recognizes biotechnology products may require additional regulation, different types of analysis and review, and, in some cases, different procedures for licensing or approval, primarily because such products may present different risks and because of the increased level of public concern about biotechnology.

An additional new aspect of the Coordinated Framework is its inclusion of several new proposed definitions, the two most significant of which are "intergeneric (new) organisms" and "pathogen." Intergeneric organisms are defined as "organisms deliberately formed to contain an intergeneric combination of genetic material,"[5] that is, organisms deliberately formed to contain genetic material from more than one genus. Specifically excluded from this definition are those organisms "that have resulted from the addition of intergeneric materials [sic] that is well-characterized and contains only non-coding regulatory regions such as operators, promoters, origins of replication, terminators, and ribosome binding regions."[6] Pathogen is defined as "a virus or microorganism (including its viruses

[2] *See* McNamara, *FDA Regulation of Food Substances Produced by New Techniques of Biotechnology*, 42 FOOD DRUG COSM. L.J. 50 (1987). *See also* Gibbs & Kahan, *Federal Regulation of Food and Food Additive Biotechnology*, 38 ADMIN. L. REV. 1 (1986). *See generally* REPORT OF HOUSE SUBCOMM. ON INVESTIGATIONS AND OVERSIGHT, COMM. ON SCIENCE AND TECHNOLOGY, ISSUES IN THE FEDERAL REGULATION OF BIOTECHNOLOGY: FROM RESEARCH TO RELEASE, 99TH CONG., 2D SESS. (1986).

[3] 51 Fed. Reg. at 23,301.

[4] The relevant federal agencies which included separate statements in the Coordinated Framework are the Envtl. Protection Agency (EPA), the Food and Drug Admin. (FDA), the U.S. Dep't of Agric. (USDA), and the Occupational Safety and Health Admin. (OSHA).

[5] 51 Fed. Reg. at 23,307.

[6] *Id.*

and plasmids, if any) that has the ability to cause disease in other living organisms."[7] Whether a product is determined to be "new" has major implications for review by each of the relevant federal regulatory agencies that will be utilizing the definitions to some degree. An organism which is viewed as "new" can be expected to undergo more intensive scrutiny, or take a longer time to be licensed or approved, and will be subject to greater burdens in terms of data requirements.

Evident throughout the Coordinated Framework statement is an emphasis on earlier federal involvement in the development of biotechnology-derived products. Federal regulation of nonfederally-funded biotechnology research, which is the source of most commercially developed biotechnology-derived products, generally commences with "deliberate release into the environment." No definitions, however, of "release into the environment" or of "containment" are proposed in the Framework. The inter-agency coordinating group, the Biotechnology Science Coordinating Committee (BSCC), will address these issues and attempt to propose definitions.[8] The recognition of the significance of these definitions by the responsible agencies and committees, and their consistent utilization, is crucial because clear definition of these terms is particularly important, and warranted, in view of the physical differences in potential for transmission of, for example, human or animal vaccines tested in the body of man or animal and pesticides sprayed on the exterior of plants or applied to soil.

The Coordinated Framework provides important recognition and support to the appropriate focus of biotechnology regulation on the products produced, and not on the process by which products are created.[9] Nonetheless, while the policy clearly reiterates the government's intent to support and expedite the approval of biotechnology-derived products, it provides, of course, no assurance the process will work rapidly. In addition, by maintaining the proper flexibility to make case-by-case decisions, the policy leaves the regulated industry and scientific communities, as well as the public and Congress, with an irreducible uncertainty as to how specific products will be reviewed and regulated from both a substantive and procedural perspective.

[7] *Id.*

[8] 51 Fed. Reg. 23,307 (1986). Both the National Institutes of Health (NIH) and individual federal agencies are also independently attempting to establish appropriate definitions for "deliberate release" within the contexts of the statutes which they administer. NIH has acknowledged that its previous definition of "deliberate release" contained in the NIH Guidelines on Research Involving Biotechnology was ambiguous. *See* NIH, Minutes of Meeting of Recombinant DNA Advisory Comm., Working Group on Definitions (Sept. 5, 1986); NIH, Memorandum to Members, Working Group on Definitions, from William J. Gartland, Jr., Ph.D., Exec. Sec'y (July 29, 1986) (setting forth the issues the group was requested to address). The U.S. Dep't of Agric., on the other hand, has previously stated in an informal internal memorandum that, with respect to animal biologics produced through biotechnology, the use of such products in normal animal husbandry practices does not constitute "deliberate release." *See* USDA, Veterinary Services Memorandum 800.68 (Dec. 4, 1984).

[9] New USDA regulations concerning the introduction of genetically-engineered plant pest products, however, depart from this focus, with these regulations in part process-based, *i.e.*, those plant pests which are genetically-engineered will be regulated differently than traditional plant pests. *See* USDA, Animal and Plant Health Inspection Serv., Final Regulation, Introduction of Organisms and Products Altered or Produced through Genetic Engineering, 52 Fed. Reg. 22,892 (1987). By contrast, a recent report of a committee of the Nat'l Academy of Sciences, INTRODUCTION OF RECOMBINANT DNA-ENGINEERED ORGANISMS INTO THE ENVIRONMENT: KEY ISSUES 7 (1987), rejects risk assessment based on the method by which the organism is produced.

The principal federal regulatory agencies likely to become involved in the regulation of biotechnology-derived products each issued a separate statement regarding its review policy.

FDA FINAL POLICY STATEMENT FOR REGULATING BIOTECHNOLOGY PRODUCTS

In its separate policy statement, the Food and Drug Administration (FDA) properly proposes to review biotechnology-derived products in essentially the same manner and utilizing the same regulatory procedures as those established for products produced by traditional (conventional) techniques.[10] Consequently, no new administrative procedures designed to address generic concerns about biotechnology in the FDA context will be promulgated by the agency.[11] Because the agency recognizes there may be differences (*e.g.*, different impurities) between products derived from biotechnology and otherwise identical traditionally produced products, the agency's principal concern in reviewing product applications will be the extent to which data submitted is adequate to establish the biotechnology-derived product is sufficiently similar or identical to the traditionally produced product that additional safety or efficacy data is not required. Because such agency determinations will be made on a case-by-case basis and testing criteria apparently will not be specified in formally promulgated agency regulations, applicants will need to devote considerable attention to the product description in their product applications. In addition, attention should be devoted to the description of adequate quality control mechanisms in order to address any agency concerns related to the utilization of biotechnology processes to produce traditional products.

In discussing the extent to which additional testing would be required for foods and food additives produced by biotechnology, the FDA policy statement indicates agency officials will consider several factors, including "the novelty of the substances used to produce the food (*e.g.*, whether a substance is an 'intergeneric' organism as defined by the initial BSCC definitions . . .), the purity of the resulting product, and the estimated consumption of the product."[12] In assessing the safety of food products, the agency also will consider whether a food derived from biotechnology contains a higher level of a substance than it would ordinarily contain or an additional harmful or deleterious substance not ordinarily contained in the food when conventionally produced. With respect to whether a generally-recognized-as-safe (GRAS) substance loses its status because it is produced or modified by biotechnology, the FDA stated "if the substance (and its contaminants) have been altered in such a way that it can no longer be generally recog-

[10] 51 Fed. Reg. at 23,309. FDA has approved numerous *in vitro* diagnostic devices and five therapeutic drug products of biotechnology to date: two versions of a human growth hormone (approved Oct. 17, 1985 and Mar. 8, 1987); human insulin (approved Oct. 28, 1986); alpha interferon (approved June 4, 1986); a monoclonal antibody for renal transplants (approved June 19, 1986); and a hepatitis-B vaccine (approved July 23, 1986).

[11] 51 Fed. Reg. at 23,309.

[12] 51 Fed Reg. at 23,313.

nized by qualified experts to be safe. . . . the substance would be a food additive and . . . must be the subject of an approved food additive regulation."[11]

With respect to animal feeds, the FDA policy statement indicates substances used in animal feeds, other than drugs, that are produced by recombinant DNA technology will be considered food additives and will require approval of a separate food additive petition, even though similar substances are currently approved as food additives.[14] Consequently, the option of establishing similarity to currently approved substances without the need to obtain separate agency approval does not appear to be available to manufacturers utilizing biotechnology to produce animal food additives. The FDA statement did not provide a justification for the differential treatment assertedly to be given to human food additives and animal food additives.

USDA FINAL POLICY STATEMENT FOR RESEARCH AND REGULATION OF BIOTECHNOLOGY PROCESSES AND PRODUCTS

Like FDA, the U.S. Department of Agriculture (USDA) reiterated in its final policy statement that it intends to regulate biotechnology processes and products within its existing regulatory framework. However, USDA has not yet developed specific policies for the regulation of meat and poultry products produced through biotechnology processes or produced from animals exposed to biotechnology products, or for seeds. USDA outlined in some detail the degree of review intended for certain types of biotechnology-derived veterinary biologics and plant pests.[15] As part of its discussion on its regulation of veterinary biologics, USDA also set out definitions of certain key terms, including "recombinant-DNA-derived products" and "vector,"[16] in an attempt to identify those processes which properly should be reviewed and approved as recombinant products. Like FDA with respect to human and animal drugs, USDA has traditionally considered veterinary biologics to present insignificant environmental risks since such products are biologically and physically contained within the host animal. However, in response to recent judicial challenges, USDA is likely to require license applicants to prepare and submit detailed environmental assessments prior to license approval.[17]

With respect to plants and plant pests, USDA established broad definitions of "regulated articles," "introduction," and "release" into the environment to encompass biotechnology-derived plants and plant pests.[18] Both USDA and the En-

[11] *Id.*

[14] 51 Fed. Reg. at 23,311.

[15] 51 Fed. Reg. at 23,341.

[16] 51 Fed. Reg. at 23,340.

[17] *See* Foundation on Economic Trends v. Lyng, Civ. No. 86-1130 (D.D.C., filed Apr. 26, 1986), discussed *infra*. The authors are counsel to the vaccine developer with respect to this litigation.

[18] 51 Fed. Reg. at 23,342–43. *See also* USDA, Animal and Plant Health Inspection Serv., Final Regulation, Introduction of Organisms and Products Altered or Produced through Genetic Engineering, 52 Fed. Reg. 22,892 (1987) and NIH, Notice of Proposed Actions under NIH Guidelines for Research Involving Recombinant DNA Molecules, 52 Fed. Reg. 29,800 (1987), incorporating proposed changes developed by USDA to include guidelines for research involving whole plants and animals.

vironmental Protection Agency (EPA) have taken the position that biotechnology-derived plants and plant pests must be reviewed independently by each agency,[19] which can be expected to result in additional delay for product testing or introduction. Neither agency, however, has addressed such issues as how to resolve differences in agency decisions concerning the pathogenicity of the same organism, whether there will be a lead agency with respect to a product, or how the different agency data requirements may affect applicants. The USDA policy statement also indicates an Agriculture Biotechnology Recombinant-DNA Advisory Committee (ABRAC) will be established.[20] However, no indication is given of the circumstances under which ABRAC review will be utilized or required, or of the membership of the committee. This lack of specificity as to the role and function of ABRAC may lead to the same types of questions which have been the subject of legal challenges to USDA in the past with respect to the consistency of agency review of biotechnology products.[21]

EPA STATEMENT OF POLICY FOR REGULATING BIOTECHNOLOGY PRODUCTS

The two principal statutes under which the EPA may regulate biotechnology products are the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)[22] and the Toxic Substances Control Act (TSCA).[23] FIFRA is a licensing statute which requires all pesticides sold in the United States to receive prior licensing approval from EPA. Under that statute, experimentation with pesticides prior to commercialization may also require licensing pursuant to EPA regulations.[24]

In its Coordinated Framework statement, EPA altered its interim policy which required that any environmental release of any genetically engineered microbial pesticide, no matter how small the quantity or the experimental plot, would require prior notification to EPA.[25] Although notification for all genetically engineered microbial pesticides is still required, the agency has divided the notification requirements into two levels consistent with the definitions of intergeneric and pathogenic organisms in the OSTP general policy statement in the Coordinated Framework. For nonintergeneric and nonpathogenic pesticides, EPA is requiring the submission of only abbreviated information to accompany the notification and has stated it will complete its review of such information within thirty days.[26] If the notifier does not receive a response from EPA within thirty days,

[19] 51 Fed. Reg. at 23,343.

[20] 51 Fed. Reg. at 23,338.

[21] *See* Foundation on Economic Trends v. Lyng, Civ. No. 86-1130 (D.D.C. filed Apr. 26, 1986) (allegations that USDA failed to obtain review of approval of recombinant-derived pseudorabies vaccine by proper USDA biotechnology review committee). *See also* Advanced Notice of Proposed USDA Guidelines for Biotechnology Research, 51 Fed. Reg. 23,367 (1986) (guidelines for review of agency-funded research).

[22] 7 U.S.C. §§ 136–136y (1982).

[23] 15 U.S.C. §§ 2601–2654 (1982).

[24] 49 Fed. Reg. 40,659 (1984); 49 Fed. Reg. 50,885 (1984).

[25] 49 Fed. Reg. 40, 659 (1984); 49 Fed. Reg. 50, 885 (1984).

[26] 51 Fed. Reg. at 23,321.

field experimentation may commence. However, EPA reserves its right to respond to such notifications by requesting more complete information or data, or by requiring the applicant to receive an experimental use permit before beginning field experiments. Intergeneric or pathogenic pesticides will demand greater agency scrutiny and, therefore, EPA is requiring more detailed information and data with the notification and has given itself a longer review period (ninety days) to respond to such notification.[27]

While the general authority of EPA to regulate genetically engineered pesticides under FIFRA appears clear, the authority to regulate other genetically engineered microorganisms under TSCA is not. This lack of clarity, combined with the status of TSCA as a notification statute rather than a licensing statute, resulted in the establishment of a less extensive and detailed regulatory framework under TSCA. EPA's statement concerning the regulation of genetically engineered substances under TSCA proposes intergeneric microbials be reviewed as "new" organisms and, therefore, subject to the premanufacturing notice (PMN) provisions of section 5 of TSCA.[28] With respect to genetically engineered substances which are not intergeneric or "new" organisms, *i.e.*, intrageneric organisms, EPA has proposed to require notification of "significant new uses" (SNUR) of those organisms only if they are pathogenic.[29] However, because EPA has not yet promulgated final regulations pursuant to its "significant new use" framework, EPA is requesting voluntary notification of such releases. Finally, the agency is planning to promulgate a rule pursuant to section 8(a) of TSCA[30] to require reporting and recordkeeping activities for all microorganisms subject to TSCA which are not otherwise reviewed under the PMN and SNUR policies.[31] This general information would be required prior to any environmental release.[32]

CURRENT JUDICIAL AND ADMINISTRATIVE CHALLENGES TO THE FEDERAL REGULATION OF BIOTECHNOLOGY

Equally significant to the development and introduction of biotechnology-derived products is the recent emergence of judicial and administrative challenges to the conduct by the federal agencies of their regulatory review functions. Because, until 1978, the National Institutes of Health (NIH), which has been principally responsible for monitoring federal research in biotechnology, expressly prohibited the deliberate release of recombinant DNA organisms,[33] there was relatively little occasion for judicial or administrative challenges. In 1978, NIH made significant revisions to its 1976 Guidelines, including the provision of waiver authority to the NIH Director to allow, with the advice of the NIH Recombinant DNA Advisory Committee (RAC), the deliberate release of recombinant or-

[27] *Id.*
[28] 51 Fed. Reg. at 23,325; 15 U.S.C. § 2605.
[29] 51 Fed. Reg. at 23,329.
[30] 15 U.S.C. § 2607(a).
[31] 51 Fed. Reg. at 23,316.
[32] 51 Fed. Reg. at 23,331.
[33] 41 Fed. Reg. 27,902, 27,907 (1976) (Recombinant DNA Research Guidelines).

ganisms.[34] The revisions also stated that the necessity for the preparation of an environmental assessment (EA) or environmental impact statement (EIS), pursuant to the National Environmental Policy Act (NEPA),[35] concerning a decision to allow a proposed deliberate release would be evaluated on a case-by-case basis.[36] NIH's evolution of its criteria for the approval of deliberate release experiments, and its influence on other federal-agency regulation of deliberate releases of biotechnology-derived products, further stimulated the commercial development and distribution of biotechnology products and provided the occasions for judicial or administrative challenge.

The tortuous history of the judicial and administrative challenges to testing of the "ice-minus" bacteria product is illustrative of the potential for serious disruption by reason of such challenges. On June 1, 1983, the NIH Director gave final approval to the first proposed field-testing in northern California of Pseudomonas syringe, a genetically-altered bacteria intended to delay frost formation on potatoes, tomatoes, and beans.[37] The approval of the field tests, which were scheduled to begin in May 1984, was challenged by Jeremy Rifkin, President of the Foundation on Economic Trends (F.E.T.), a small "public interest" organization, in federal district court in September 1983, on the basis NIH had violated provisions of the Administrative Procedure Act (APA)[38] and NEPA. The district court issued a preliminary injunction enjoining NIH and the University of California Regents from conducting the experiments and enjoining the NIH from approving all other deliberate releases of DNA organisms.[39] On appeal, the U.S. Circuit Court of Appeals for the District of Columbia affirmed the lower court's finding that the NIH had completely failed to consider the possibility of various environmental effects of the proposed field test, especially the risks concerning possible dispersion of the bacteria into the environment and, thus, had failed to fulfill its statutory obligations pursuant to NEPA.[40] The court's decision was based on evidence the NIH RAC's consideration of the dispersion issue, which was documented by one sentence from the minutes of two RAC meetings in which the field test was reviewed, was inadequate. The minutes indicated that during those two meetings, dispersion of the bacteria was considered once and the RAC conclusion, taken almost verbatim from the test sponsor's proposal, was that the possibility of dispersion posed little or no environmental risk.[41] Without more, the court concluded, it had no alternative but to find the NIH had not satisfied its NEPA obligations. This challenge, and the success of it, illustrated the potential for the use of environmental assessment obligations under NEPA to provide the

[34] 43 Fed. Reg. 60,108 (1978). The 1978 revisions also extended the applicability of the 1976 Guidelines to all experiments at institutions receiving NIH funds for rDNA research, whether or not the experiment in question had been directly funded by NIH. *Id.* at 60,123.

[35] 42 U.S.C. §§ 4321–4370a (1982).

[36] 43 Fed. Reg. 33,042, 33,051 (1978) (preamble to 1978 proposed revised guidelines).

[37] 48 Fed. Reg. 24,548, 24,549 (1983).

[38] 5 U.S.C. §§ 702, 706 (1982).

[39] Foundation on Economic Trends v. Heckler, 587 F. Supp. 753 (D.D.C. 1984).

[40] Foundation on Economic Trends v. Heckler, 756 F.2d 143, 153 (D.C. Cir. 1985).

[41] *Id.* at 153.

basis for judicial challenge to similar experiments, both publicly and privately funded.

F.E.T. again challenged proposed field-testing of the ice-minus bacteria in November 1985, when EPA granted an experimental use permit (EUP) under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) to a commercial firm, Advanced Genetic Sciences, Inc. (AGS), to field test the bacteria on strawberry plants, alleging EPA violations of the APA and NEPA.[42] However, due to local opposition to the field-testing and because AGS had apparently already conducted limited tests with the bacteria, EPA suspended the EUPs and fined AGS $13,000 for failing to adequately report the experiments, which EPA concluded were "deliberate releases."[43] The F.E.T. complaint was then voluntarily dismissed without prejudice based on the suspension of the permits.[44] The district court held, however, if the agency reinstated the EUPs, the court of appeals would be the proper forum for review.[45] Thus, any future challenges to AGS' field-testing of ice-minus bacteria will be reviewed on the administrative record before the court of appeals, rather than by *de novo* review by the district court.

Subsequent to EPA's suspension of the EUPs for the AGS field-testing, the agency announced it was approving similar field-testing of ice-minus by University of California scientists on two one-acre potato fields in northern California leased by the University.[46] In this instance, F.E.T. and local environmental groups filed a motion for a temporary restraining order in California state court, alleging approval of the test by EPA and the state Department of Food and Agriculture violated the California Environmental Quality Act.[47] Although the University argued that state law requirements were superceded by federal law, and that, in addition, the field tests posed no environmental threat, it nevertheless agreed to reconsider whether it had adequately assessed the potential environmental effects of the test.[48] Because of the timing of the field test during the planting season, the University, in essence, agreed to postpone the tests to the next planting season. Such litigation is illustrative of the potential use of state and local laws and regulations in providing a basis for challenges to development or introduction of biotechnology-derived products, even in instances when the activity may not have been challenged in a federal forum.

Another product specific judicial challenge which F.E.T. instituted, *Foundation on Economic Trends v. Lyng*,[49] involves a pseudorabies vaccine for swine, approved for commercial distribution by USDA, Veterinary Services, as an an-

[42] Foundation on Economic Trends v. Thomas, Civ. No. 85-3639 (D.D.C. filed Jan. 27, 1986).

[43] Chem. Reg. Rep. (BNA), Current Rep. at 1635 (Mar. 28, 1986).

[44] *Id.*

[45] *Id.* EPA on Sept. 7, 1986, subsequently reinstated the EUPs to allow AGS to conduct field tests with ice-minus bacteria, pending agency review of an appropriate test site.

[46] Chem. Reg. Rep. (BNA), Current Rep. at 601 (Aug. 8, 1986).

[47] *Id. See* Californians for Responsible Toxic Management v. Regents of The Univ. of Cal., No. 342097 (Sacramento County Super. Ct., order filed Aug. 1, 1986).

[48] Chem. Reg. Rep. (BNA), Current Rep. at 682 (Aug. 22, 1986).

[49] Foundation on Economic Trends v. Lyng, Civ. No. 86-1130 (D.D.C. filed Apr. 26, 1986). As noted above, the authors are counsel to the vaccine developer with respect to this litigation.

imal biologic under the Virus-Serum-Toxin Act.[50] Although the legal bases for the challenge to the vaccine approval were identical to those claims made in the ice-minus litigation, *i.e.*, violations of the APA and NEPA, the approval was not challenged until four months after its manufacturer had commenced commercial distribution. Initially, F.E.T. asserted USDA had failed to document in a formal manner the environmental assessment under NEPA of its approval of the vaccine.[51] The agency, in conjunction with the vaccine manufacturer, agreed to voluntarily suspend distribution of the vaccine for a two-week period pending USDA's formalization and publication of its internal environmental assessment.[52] Upon publication of the USDA's assessment and confirmation of its decision that approval of the vaccine did not present a significant environmental impact,[53] F.E.T. instituted litigation.[54]

The *Lyng* litigation highlights several additional issues with respect to product approvals which all federal agencies involved in approving biotechnology products should address to reduce the possibility of future challenges to their activities. Principal among these issues is the establishment of clear and concise definitions concerning "recombinant DNA organisms," including whether the term includes simple gene deletion techniques, and "deliberate release," including whether the term includes the administration of a recombinant DNA product to humans or animals. Further, federal agencies should establish consistent and uniform procedural frameworks for the review and approval of biotechnology products which incorporate clear criteria concerning the scope and nature of internal agency review and documentation. Avoidance of the appearance of post-hoc rationalization in decisionmaking will also serve to reduce the potential for successful judicial challenge.

In addition to challenges to product specific approvals, recent litigation has involved more general biotechnology programs of several agencies. For example, in *Foundation on Economic Trends v. Weinberger*,[55] the plaintiff was successful in persuading the district court to issue a permanent injunction enjoining the construction of proposed aerosol and toxic agent test support facilities until the Department of Defense (DOD) prepared an adequate EIS. The court held the mere contemplation by DOD that in the future it might use the facilities to test toxins produced through genetic engineering was not sufficient in itself to require the preparation of an EIS.[56] Nevertheless, because the remainder of DOD's environ-

[50] 21 U.S.C. §§ 151–159 (1982).

[51] Petition from Jeremy Rifkin, Pres., Found. on Economic Trends to Sec'y, U.S. Dep't of Agric.; Adm'r, Animal and Plant Health Inspection Serv.; and J. K. Atwell, Dep'y Adm'r, Veterinary Servs., U.S. Dep't of Agric. (Apr. 3, 1986).

[52] Letter from Bert W. Hawkins, Adm'r, Animal and Plant Health Inspection Serv., U.S. Dep't of Agric., to Edward Lee Rogers, Esq., Counsel for Found. on Economic Trends (Apr. 8, 1986).

[53] U.S. Dep't of Agric., "Environmental Assessment and Finding of No Significant Impact," 51 Fed. Reg. 15,657 (1986).

[54] Because the plaintiffs did not seek a preliminary injunction, the vaccine continues to be marketed; no adverse environmental incidents from use have been reported. *See* Defendant's Motion for Summary Judgment, Affidavit of Dr. George Shibley at 20, Foundation on Economic Trends v. Lyng (Civ. No. 86-1130) (D.D.C. filed Apr. 26, 1986).

[55] 610 F. Supp. 829 (D.D.C. 1985).

[56] *Id.* at 840.

mental assessment contained mere conclusory statements about the potential environmental impact of the new facilities, the court held the assessment did not satisfy the "hard look" standard of review under NEPA and, therefore, was inadequate.[57] In a similar challenge against DOD activities, *Foundation on Economic Trends v. Weinberger*,[58] DOD agreed to prepare an environmental impact statement with respect to its biological defense research program.[59] Although the Department did not admit in the settlement an EIS was legally mandated by NEPA in this case,[60] DOD's agreement to prepare an EIS will likely serve, as a practical matter, as precedent for the standard of environmental review for future DOD recombinant DNA research and testing programs.

In addition to DOD programs, USDA and EPA biotechnology programs have also been challenged in recent litigation. In *Foundation on Economic Trends v. Block*,[61] the district court granted summary judgment to the USDA Agricultural Research Service (ARS), rejecting F.E.T.'s allegations of violations of the APA and NEPA in connection with certain ARS-sponsored livestock productivity studies involving genetic engineering. Because the research was performed on a small scale and was limited to contained facilities, *i.e.*, performed under laboratory conditions with ample security, the court held the animal productivity studies did not constitute a proposal for major federal action and, by definition, contained studies which could have no environmental impact.[62] Therefore, an environmental assessment prepared at such a preliminary stage of the research would result in nothing more than an "unfounded hypothesis."[63] The court observed plaintiffs' complaint concerning the propriety of ARS' involvement in genetic-engineering research was more properly addressed to Congress than to the courts.[64]

For reasons similar to those in the *Block* decision, the district court in *Foundation on Economic Trends v. Johnson*[65] granted the government's motion to dismiss F.E.T.'s challenge to the Coordinated Framework itself. The court held plaintiffs' APA and NEPA claims were not well-founded and were premature, in that the Framework is not a legally binding regulation but, rather, a guideline for future agency regulation. Any predictions with respect to the regulatory policies individual agencies might follow based on the Framework were, therefore, highly speculative and not ripe for judicial review.[66] Further, the court held plaintiffs had not demonstrated the requisite standing requirements of actual injury, causation,

[57] *Id.* at 841–42.

[58] Foundation on Economic Trends v. Weinberger, Civ. No. 86-2436 (D.D.C. filed Sept. 23, 1986); (order entered Feb. 18, 1987) (settlement unpublished).

[59] *See* 6 Biotech. L. Rep. (Lieber) 178 (Mar.–Apr. 1987).

[60] *Id.*

[61] Foundation on Economic Trends v. Block, Civ. No. 84-3045 (D.D.C. opinion and order filed Apr. 29, 1986); *see* 5 Biotech. L. Rep. (Lieber) 177 (May–June 1986).

[62] 5 Biotech. L. Rep. at 186.

[63] *Id.* at 187.

[64] *Id.*

[65] Foundation on Economic Trends v. Johnson, Civ. No. 86-1590 (D.D.C. opinion filed Dec. 22, 1986).

[66] *Id.* slip op. at 6.

and redressability.[67] Similar deficiencies in meeting the actual injury requirement for standing and a lack of ripeness led to dismissal of the complaint in *Foundation on Economic Trends v. Thomas*.[68] In that case, F.E.T. challenged EPA's denial of F.E.T.'s administrative petition that the agency, through rule-making procedures, establish criteria to require applicants for environmental use permits under FIFRA to demonstrate financial responsibility in the event of adverse environmental consequences from the release of recombinant organisms, as a precondition to issuance of a permit.[69]

Because most FDA-regulated products derived from biotechnology have been drugs or devices, which generally do not engender a significant degree of concern with respect to environmental release, only one action has been filed at this writing concerning the agency's regulatory review activities regarding a biotechnology-derived product. That case, *Foundation on Economic Trends v. Department of Health and Human Services*,[70] demands release of FDA environmental assessment records relating to investigational new animal drug applications (NADAs) concerning bovine somatotropin. In April 1986, F.E.T. submitted a citizen petition to FDA requesting the agency prepare an environmental impact statement before approving the proposed field testing of bovine somatotropin, also known as bovine growth hormone (BGH), in dairy cattle.[71] The citizen petition asserted FDA approval of BGH would: (1) significantly affect agricultural land use in milk-producing regions of the United States; (2) adversely affect the internal environment of cattle injected with BGH; and (3) have adverse economic and social impacts on the dairy industry.[72] FDA denied the petition, stating that, under its confidentiality regulations, it is "unable to disclose the existence or non-existence of NADAs and therefore is unable to disclose the status of environmental reviews until applications are approved."[73] FDA added, to the extent the petition requested the preparation of an EIS independently of the new animal drug approval process, the petition was denied because NEPA, and its EIS re-

[67] *Id.* slip op. at 7.

[68] Foundation on Economic Trends v. Thomas, Civ. No. 86-1590 (D.D.C. opinion filed Dec. 30, 1986).

[69] *Id.* slip op. at 10. One commentator has argued, unconvincingly in our view, in favor of imposition of a mandatory insurance requirement on biotechnology firms, notwithstanding the serious current difficulties in obtaining insurance coverage for health care industry activities, the significant costs likely to be associated with such a requirement, and the likely adverse effects on competition that can reasonably be expected from such a requirement. *See* Note, *Designer Genes that Don't Fit: A Tort Regime for Commercial Release of Genetically-Engineered Products*, 100 HARV. L. REV. 1086, 1093–99 (1987).

[70] Foundation on Economic Trends v. Dep't of Health and Human Servs., Civ. Action No. 87-1009 (D.D.C. filed Apr. 10, 1987).

[71] Letter from Edward Lee Rogers, Esq., counsel for F.E.T., to John Matheson, FDA, with enclosed citizen petition, Docket No. 86P-0148 (Apr. 1, 1986).

[72] *Id.* at 2–3. F.E.T. also attempted to generate congressional interest in its proposal that FDA and USDA jointly prepare an environmental impact statement. *See* Letter from Jeremy Rifkin, Pres., Found. on Economic Trends, to Frank Young, Comm'r, FDA, and Richard Lyng, Sec'y, U.S. Dep't of Agric. (June 23, 1986).

[73] Letter from John M. Taylor, Acting Assoc. Comm'r for Regulatory Affairs, FDA, to Jeremy Rifkin, Pres., Found. on Economic Trends (Sept. 29, 1986).

quirements, apply only to proposed actions.[74] Following denial of its petition, F.E.T. filed its complaint demanding release of environmental assessment information in FDA's possession.

These judicial challenges are indicative not only of the creativity of opponents of development of biotechnology but, more significantly, of the range of objections which may be advanced in judicial challenges. Even though many of these challenges have been unsuccessful, the possibility of such challenges can be expected to result in additional agency delay and further procedural requirements. Because of the potential for such challenges, companies contemplating field-testing or commercial distribution of products derived from biotechnology processes must begin to include in their product development process clear documentation of internal scientific and environmental review of the product prior to release, whether or not legally required, to provide a basis to reduce the risk of successful judicial or administrative challenges. Further, companies contemplating development and marketing of biotechnology products must also monitor the review activities of the relevant federal agency to reduce, to the extent practicable, the opportunity to initiate judicial or administrative challenges based on a failure to adhere to the agency's procedural requirements.

CURRENT ISSUES REGARDING THE REGULATION OF BIOTECHNOLOGY

Notwithstanding this substantial recent litigation, several central issues relating to the regulation of biotechnology remain unresolved. Primary among these is delineation of the scope of products which are to be regulated. Such delineation will remain difficult as long as several key terms remain undefined, ambiguous, or proposed, but not adopted. These key terms include "deliberate release into the environment," "intergeneric organism," "pathogen," "recombinant DNA" technology, and "containment." The NIH Recombinant DNA Advisory Committee has acknowledged the ambiguity of two of these terms, "deliberate release into the environment" and "recombinant DNA molecule," and is currently attempting to define them more precisely.[75]

Clear and acceptable definitions are crucial to a successful regulatory program, from both the industry and government perspectives. With respect to regulation of food and food additive products, for instance, FDA has yet to establish clear parameters for deciding when a novel food/food additive exists as opposed to a traditional food/food additive derived from biotechnology. Without such parameters, it is unclear when agency review needs to be requested or is required for traditional products which can now be derived from biotechnology. Further, al-

[74] *Id.* at 3. Recently, the F.E.T. submitted a citizen petition to FDA questioning the scientific and statistical validity of the current testing of bovine somatotropin and requesting FDA to initiate and financially support independent research on the safety, efficacy, and economic consequences of using bovine somatotropin. *See* Citizen Petition from Jeremy Rifkin, Pres., Found. on Economic Trends, to Frank Young, Comm'r, FDA, Docket No. 87P-0318 (Sept. 16, 1987).

[75] *See* Report of NIH Committee to Review Allegations of Violations of the NIH Guidelines for Research Involving Recombinant DNA Molecules in the Conduct of Field Tests of a Pseudorabies Vaccine at Baylor College of Medicine and/or Texas A&M Univ. (Oct. 9, 1986); *see also supra* note 8 (discussion of NIH attempts to establish more precise definitions of key terms).

though the agency has indicated that GRAS food ingredients, for example, can lose their GRAS status when produced through biotechnology, the agency has issued no guidance with respect to how manufacturers are to test or assess for new impurities in the final food product or even if that is the sole or principal focus of the agency's concern.[76] Consequently, in addition to the establishment of concise definitions, it is imperative for the agency to issue useful specific guidelines for assessment in this area, similar to the "Points to Consider" documents prepared by FDA for drug products derived from biotechnology.[77]

As others have observed,[78] until FDA issues such guidance, food and food additive manufacturers will be required to make decisions with respect to regulatory strategies based on analogous regulatory procedures. In the food area, it therefore appears a manufacturer could rely on a self-claimed approval status for a substance produced by biotechnology which is "substantially identical" to a traditionally produced food or GRAS substance, or which is already approved by an existing food additive regulation for the conventionally produced product. Based on the agency's treatment of a recent GRAS status affirmation petition filed by CPC International for use of the enzyme *alpha* amylase derived from modified *Bacillis subtilis*,[79] it appears the agency properly will allow reasonable discretion in making such determinations.

The potential to make such determinations in the food/food additive area contrasts with FDA's position in its Coordinated Framework statement that new food additive petitions will be required for all substances used in animal feeds which are produced through recombinant DNA technology, even though a similar substance is currently approved as an animal food.[80] This position raises several unresolved issues including what statutory basis exists under the Federal Food, Drug, and Cosmetic Act for any such differential regulatory treatment between human and animal food additives. Similarly, a question is raised whether such a position with respect to animal feeds would be improperly discriminatory to domestic manufacturers in the event a biotechnology production process for imported products could not be discerned in final product sampling.

Although such unresolved issues will have significant commercial implications with respect to the cost of developing and marketing a biotechnology food or food

[76] *See, e.g.*, 21 C.F.R. § 170.30(f), noting FDA will review GRAS status where there are "significant alterations" in the food substance. With respect to drug product identity and impurities, *see* Lasagna, *Clinical Testing of Products Prepared by Biotechnology*, 6 REG. TOX. & PHARM. 385, 386 (1986).

[77] *See, e.g.*, FDA Center for Drugs and Biologics, "Points to Consider in the Production and Testing of New Drugs and Biologicals Produced by Recombinant DNA Technology" (draft, Apr. 10, 1985). *See also* J. H. Maryanski, Biotechnology Coordinator, Center for Food Safety and Applied Nutrition, FDA, Remarks at Food and Biotechnology Int'l Symposium, Univ. of Laval, Quebec, Canada 6–9 (Aug. 21, 1986) (available upon request from FDA).

[78] *See generally* Gibbs & Kahan, *Federal Regulation of Food and Food Additive Biotechnology*, 38 ADMIN. L. REV. 1 (1986); Knudsen, *Potential Food Safety Problems in Genetic Engineering*, 5 REG. TOX. & PHARM. 405 (1985); McNamara, *FDA Regulation of Food Substances Produced by New Techniques of Biotechnology*, 42 FOOD DRUG. COSM. L.J. 50 (1987).

[79] 51 Fed. Reg. 10,571 (1986) (notice of filing of GRAS affirmation petition.) *See also* FOOD CHEM. NEWS, Nov. 3, 1986, at 32 (announcement by CPC that, with expiration of comments with no comments filed, FDA has agreed with the company that the substance can be deemed to be GRAS).

[80] 51 Fed. Reg. 23,301, 23,311 (1986).

additive product, these issues also, and more importantly, raise potential implications concerning the perceived integrity and safety of the food supply. For conventionally-produced foods and food additives which are GRAS, there is no premarket approval requirement. Food or food additive products derived from biotechnology which are substantially similar or identical to the conventionally-produced products appear properly subject only to postmarket review under the general food adulteration and misbranding provisions.[81] Whether FDA will be willing to rely on these enforcement mechanisms as the sole means of regulating such biotechnology-derived food products is unclear, particularly in view of possibly conflicting public expectations or attitudes with respect to the proper degree of regulation in this area.

PRACTICAL CONSIDERATIONS FOR THE INTRODUCTION OF BIOTECHNOLOGY PRODUCTS

At present, the timing and quality of the relevant agency's environmental assessment of its decision approving development or introduction of biotechnology-derived products are most significant to the likelihood of successful defense to any challenge to an agency's action. The significance of the environmental assessment requirement under NEPA, and of the vulnerability of biotechnology research and product introduction to challenges under NEPA, was not generally foreseen.[82] In view of the significant risk of challenge on this basis, however, both the regulatory agencies and the regulated industry must be attentive to: (1) compliance with internal agency procedures as to the time of preparation of environmental assessments, making certain the agency has ample time to review and document its environmental assessment; (2) clarity and consistency of these internal agency procedures; and (3) adequate coverage and content of the environmental assessment, making certain the agency has the data and background information to arrive at and document its decision with respect to the environmental risk or lack thereof posed by the product approval. As a practical matter, the burden of meeting the NEPA requirements will generally fall on the regulated industry. Manufacturers of biotechnology products must be prepared to incorporate into their product development strategies and budgets adequate consideration of, and resources for, the preparation of environmental assessments. Express consideration must be given to the possibility of, and principal focus of, possible judicial or administrative challenges.

Product development strategy must also incorporate consideration of potential agency jurisdictional conflicts, *e.g.*, between USDA/FDA, EPA/FDA, and USDA/EPA, which may delay and/or make more costly biotechnology research and product introduction through imposition of substantially different data re-

[81] 21 U.S.C. §§ 342, 343 (1982).

[82] *See, e.g.*, Korwek, *Recombinant DNA and the Law: Review of Some General Legal Considerations*, 15 GENE 1, 3 (1981) ("[T]o meet the requirements of NEPA, manufacturers of products utilizing the recombinant DNA technology would simply have to provide evidence of no adverse environmental effects").

quirements and by using substantially different approval procedures. To reduce the potential disruption of such jurisdictional conflicts, early contact should be established with agency officials in order to delineate jurisdictional boundaries. Close attention must also be given to the description of the intended uses of the proposed product in order, to the extent practicable, to assist in the determination of which agency will take the lead with respect to review and approval of the product.

Finally, both the regulating agencies and regulated industry must recognize that many of the recent judicial and administrative challenges to biotechnology products or programs have been brought by individuals or organizations opposed to the introduction of any biotechnology products. They are not, therefore, traditional litigation or negotiation adversaries reasonably amenable to compromise settlement. Such recognition must be incorporated into the regulatory and litigation strategies of both the government and industry. With respect to all of these issues, public perception of the scientific validity and regulatory adequacy of review of biotechnology-derived products is crucial. As the Office of Technology Assessment has concluded, public perception is likely to play a central role in whether the United States maintains or forfeits its current leadership in biotechnology.[83] In the event of significant public concern with the adequacy of agency safety assessments, congressional action imposing further requirements on the development and introduction of biotechnology-derived products can be expected.

[83] *See* OFFICE OF TECHNOLOGY ASSESSMENT, COMMERCIAL BIOTECHNOLOGY: AN INTERNATIONAL ANALYSIS 498–99 (Jan. 1984). For a comprehensive recent survey of public attitudes, *see* OFFICE OF TECHNOLOGY ASSESSMENT, NEW DEVELOPMENTS IN BIOTECHNOLOGY — BACKGROUND PAPER: PUBLIC PERCEPTIONS OF BIOTECHNOLOGY (May 1987). *See also* NAT'L RESEARCH COUNCIL, AGRICULTURAL BIOTECHNOLOGY: STRATEGIES FOR NATIONAL COMPETITIVENESS (1987).